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THE STRUCTURE OF INTRAORAL CARCINOMA IN RELATION TO RADIOSENSITIVITY, TISSUE DOSAGE AND ADEQUATE THERAPY*†

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FOR many years a certain relation has been known to exist between the histological structure of a given tumor and its behavior under radiation. This relation does not necessarily apply to all varieties of malignant disease or to similar types of tumors under different anatomical settings. Similar tumors in similar anatomical settings may behave differently in different individuals. Metastases and extensions from a tumor do not necessarily exhibit the same radiosensitivity as does the primary tumor. In any given tumor the behavior under irradiation is dependent on the fundamental nature (tissue of origin) of the tumor, its location, its cellularity, its degree of anaplasia, its vascularity, its degree of papillary character, the nature of the tumor bed, the presence or absence of infection and the general status of the patient bearing the tumor. Tumors of different fundamental types have individual peculiarities of behavior which must and can only be established by prolonged study with the attempt to explain their idiosyncrasies.

It is easy to talk about the radiosensitivity of a given tumor but difficult to discuss it with any concrete notion of what one means. In the past, irradiation was a haphazard sort of procedure. Gross differences in tumor behavior were noted, differences so apparent that they even led to the discovery of hitherto unrecognized entities in the neoplastic group (endothelial myeloma, transitional cell carcinoma, lymphoepithelioma). But so long as radiation dosage was empirical and often either crudely measured or actually unknown there was little basis for planning out a course of clinical procedure on the basis of the known probable radiosensitivity of a given tumor type. With the extension to other branches of the tumor field of the efforts of Martin and Quimby[1] to actually calculate the dose received by a tumor over a known arbitrary period of time, much of the empiricism of radiation should disappear and it should be possible to plan before hand a schedule of treatment based upon the histology and clinical setting of a given tumor much as one calculates the quantity of digitalis necessary to digitalize a patient of a certain weight. Whereas this may appear over-optimistic it is nevertheless a step in the right direction. The effort necessary to secure sufficient data for determinations of this sort is considerable and the

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amount of required clinical material extensive, yet the end justifies the effort.

It is the purpose of the present brief communication to show by means of a few illustrative cases the behavior of certain types of intraoral carcinoma and the relation between their structure and response to irradiation. Most of these cases appear in the charts of Martin, Quimby and Pack.[2]

Case I. Male, aged 56 years, entered the hospital June 7, 1929. Eleven weeks prior to admission he noted a mass in the right cervical region. Examination revealed an ulcerated lesion involving the right tonsil, extending down into the pyriform sinus. There was a fluctuant mass 6 cm. in diameter in the deep cervical chain on the right, deeply fixed. Biopsy from the primary tumor showed typical squamous carcinoma, grade II, radioresistant. The tumor was measured in the usual manner. The dose received by the primary mass was not calculated but the dosage of the neck mass is known. The deepest portion of the node tumor received 420 per cent of an S.E.D. over a period of 20 days. This dose was nevertheless sublethal for the neck mass.

Case II. Female, aged 53 years, entered the hospital November 2, 1928. Examination revealed an ulcerated, granular lesion beginning at the left anterior tonsillar pillar and extending forward about 3 cm. It infiltrated the tongue to a depth of 1 to 1.5 cm. There was a hard, fairly movable node, 1.5 cm. in diameter just anterior to the left carotid bulb. A biopsy revealed typical adult squamous carcinoma, grade II, radioresistant. The lesions were measured in the usual manner. Treatment of both primary and metastatic lesions was by radium element pack and buried radon tubes. The primary lesion completely regressed under a dosage of 960 per cent of an S.E.D. The node received 320 per cent and this dose was proved sublethal. One is therefore justified in stating that the lethal dose for this tumor is more than 3.2 S.E.D. and lies somewhere between 3.2 and 9.6 S.E.D., probably from other experience nearer the upper than the lower level.

Both of these tumors were adult squamous carcinomas, with fully developed epithelial pearls. The maximum known *sublethal* dose for the metastatic node was 420 S.E.D. Martin, Quimby and Pack have shown that the lethal doses for 32 cases of adult squamous intraoral carcinomas range from 6 S.E.D. upward and that the probable average lethal dose lies between 8 and 10 S.E.D. They likewise find that in 24 patients with this type of carcinoma, 1 to 6 S.E.D. were sublethal. Obviously then, when the clinician receives a biopsy report of adult squamous carcinoma, no radiation treatment calculated to deliver the lower range of dosage can be considered as anything less than a palliative procedure. The aggressive curative treatment of such types as intraoral carcinoma makes the use of interstitial irradiation imperative. The rare exceptional favorable results with methods of irradiation designed to, or by their very nature restricted to the delivery of lower doses are scarcely calculated to improve the curability percentage of adult squamous intraoral cancer. Given a favorable clinical setting for aggressive curative treatment, the nature of this treatment should be regulated by the histologic structure of the tumor.

Increasing degrees of anaplasia in epidermoid carcinoma are said to be associated with increasing radiosensitivity. The following two case histories indicate that although one is dealing with more anaplastic, grade III, histologically moderately radiosensitive, epidermoid carcinomas of the intraoral cavity, one is far from safe in depending on lower doses.

Case III. Male, aged 57 years, entered the hospital June 5, 1929. Examination revealed a partly ulcerated, hard, irregular mass, 3 by 1.5 cm., located in the anterior left floor of the mouth just beginning to infiltrate the under surface of the tongue. There was a metastatic mass 3.5 by 2.0 cm. extending upward from the region of the left carotid bulb and a second in the submaxillary region. Biopsy showed epidermoid carcinoma, grade III, radiosensitive. The dose received by the primary tumor was 1500 per cent of an S.E.D. The lesion showed complete regression and has not recurred to date. The node masses received 1070 and 1130 per cent of an S.E.D. respectively. This dose was lethal for those nodes. Nevertheless five months later another node appeared in the opposite submaxillary region in a location which had received 285 per cent of an S.E.D. during the first irradiation. It must therefore be assumed that tumor had been present all along in this node and that 3.85 S.E.D. failed to destroy it. The lethal dose for this tumor must therefore exceed approximately 4 S.E.D. even

though it is a cellular anaplastic tumor and histologically moderately radiosensitive.

Case IV. Male, aged 74 years, entered the hospital on July 18, 1926. Examination revealed in the left anterior floor of the mouth a raised, ulcerated, granular lesion, 3 by 2 cm. In the left neck just below the angle of the jaw there was a hard, movable, metastatic mass, measuring 2.0 by 2.5 cm. This mass was implanted with gold tubes and received external irradiation with the emanation pack and by x-ray. Four months afterward—after both the primary tumor and the metastases had disappeared—a second metastatic node appeared in the submaxillary region. This mass was dissected and the presence of radiated carcinoma verified. The first node received 925 per cent S.E.D. The second node during the course of the initial irradiation of the primary tumor and the first node had received 540 per cent S.E.D., but, although tumor tissue showed decided irradiation changes, the dose was sublethal. The lethal dose for this grade III, rather anaplastic, squamous carcinoma of the floor of the mouth therefore exceeded 5.5 S.E.D. This result suggests that even when the tumors are quite cellular and anaplastic, it is unsafe to depend on other than fully adequate interstitial irradiation—of course coupled with external radiation—for curative purposes.

It is to be noted that all the four patients above described had tumors situated in the anterior oral cavity—anterior to the line of Waldeyer's ring. Tumors posterior to the line of the tonsillar pillar, the circumvallate papillae, the soft palate, and growths of the pyriform sinus, extrinsic larynx and nasopharynx tend to be more radiosensitive than do similar types in the anterior portion of the oral cavity. Moreover these locations comprise the favorite sites for transitional cell carcinoma and lymphoepithelioma. It is to be noted from the work of Martin, Quimby and Pack that the lethal doses for transitional cell carcinomas averages considerably less than for adult squamous carcinoma. One patient required as little as 1.4 S.E.D. to destroy the primary tumor.

The relative inaccessibility of the posterior oral cavity and extrinsic laryngeal region and the relative sensitivity of growths in this territory should encourage the radiologist, when he receives a biopsy report of a relatively or highly radiosensitive carcinoma in this region, to rely on external radiation alone for curative purposes—assuming the patient within the limits of cure. He will thereby eliminate the difficulties of approach to the lesion, the inaccuracies of gold seed implantation in an inaccessible field, the danger of uncontrollable hemorrhage, slough, and fatal aspiration pneumonia, and with methods of divided doses such as that in use by Coutard, the probability of having a fair number of cases free from disease is perhaps greater than is obtainable by any other method. Whereas certain tumors may not react satisfactorily, or may not vanish under external radiation when they might have disappeared with gold seeds, the dangers contingent upon gold seed implantation will probably outweigh in the long run any advantage they might have in some few particular cases.

The following patient illustrates what may be accomplished in the way of divided dose treatment in a transitional cell carcinoma of the larynx.

The patient was a male 66 years old. He had noted soreness of the throat, and dry cough for some 6 months. Two weeks prior to admission he raised considerable blood. A biopsy was performed on a cervical node in another hospital and the diagnosis of laryngeal carcinoma made. The right wall of the larynx was indurated. There was an irregular, fissured, partly ulcerated lesion involving mainly the right arytenoid. It extended up on the right aryepiglottic fold, over the base of the epiglottis and over the right pharyngeal wall across the commissure to involve the entire left aryepiglottic fold. The lesion measured about 3 cm. in diameter. Just posterior to the angle of the jaw was a moderately fixed mass 4 cm. in diameter. The patient was clearly inoperable. Biopsy showed a radiosensitive, grade III, transitional cell carcinoma. For this reason it was decided to treat the patient by divided doses of high voltage x-ray. This was done and 12 treatments were delivered, one each day, to the right and left neck alternately. Each dose consisted of 395 r units. The total dose to the involved area of the larynx was 4 S.E.D. A moderate superficial skin desquamation resulted. The mucous membrane was covered by a moderate amount of diphtheritic membrane. The patient's general condition remained good. Loss of weight during treatment was but 6 pounds. Within about 2 weeks after completion of treatment no disease was demonstrable in the larynx. One month later the patient presented no evidence

of disease. The dose employed is less than can be safely tolerated. This method of treatment is at present under experimental development in the intraoral department of the Memorial Hospital and promises very well. It is a clear attempt in the proper direction since it is an effort to apply known radiological principles to a disease of known average behavior.

CONCLUSIONS

Squamous carcinoma of the anterior oral cavity should not be treated by external radiation alone with the idea of curing the disease. These tumors resist in general any external irradiation which is within the patient's tolerance.

Epidermoid carcinomas of the posterior oral cavity, nasopharynx, pyriform sinuses and extrinsic larynx, provided these tumors are not fully developed adult squamous cancers, justify curative attempts by external radiation alone, since these tumors are relatively radiosensitive and since their situation is unfavorable in many respects for the use of interstitial irradiation. In other words, the treatment of carcinoma in these locations should be determined by the result of biopsy examination tempered by sound clinical judgment.*

* For discussion, see page 39.

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THE TREATMENT OF ORAL CANCER*

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THE following report is based chiefly on the experience in the treatment of oral cancer, excluding cancer of the lip and antrum, at the Collis P. Huntington and Massachusetts General Hospitals. The figures given are those obtained from an analysis of this group of cases observed during the six year period, 1918–24, 763 in number. It has been the custom at these institutions to study groups of cases of cancer at approximately 3 year intervals, the cases that have been treated at least five years before being collected, analyzed and the results of treatment noted. The 3 year group from 1924 to 1927 is now being studied, while the results of the cases observed from 1918[1] to 1924[2] have previously been published.

The rules adopted by the Committee on Cancer of the American College of Surgeons have been adopted in studying this group and no case is spoken of as a cure unless 5 years have elapsed since the last treatment and unless the diagnosis has been confirmed by pathological examination of the tissues. These rules are commonly accepted in studying groups of cases treated surgically, and although it is more difficult to conform to the same standard in cases treated by other methods there is no reason why it should not be applied. Cases reported as "well" 6 months to 3 years after treatment are of no value whatever in determining the efficacy of that form of treatment. The report of one or a few patients treated by a given method is also of no value, as there is always the unusual or exceptional case.

The cards advocated by the Committee have been used in making this study and their classification adopted. For the information of those not familiar with this classification, I may say that the cases are divided into two main groups, primary and recurrent, and the primary cases further divided into those with and those without evidence of glandular metastases at the first consultation. If these rules are strictly adhered to and the arrangement of the cards followed in reporting the results of treatment of groups of cases it allows comparison of cases treated by different methods, and at different institutions which is now impossible.

Certain etiological facts of interest were brought out in studying the cases. Chronic irritation such as the use of tobacco, as chewing or smoking, poorly fitting dental appliances or other foreign bodies was a definite etiological factor. Leucoplakia was noted as present in over 20% of the cases, and many of these had a positive Wassermann test. In the group as a whole the Wassermann was taken in 411, and was positive 18.7%. In other words, irritation, leucoplakia and syphilis are of distinct etiological significance.

The term cancer is a very general one. The rapidity of growth and method of spread, as we all appreciate, are entirely different in cancer in different organs. Cancer of the tongue is on the whole a rapidly growing type and is often incurable in a few months. The duration of the primary case is shown in the following table. (Table 1)

TABLE 1

AVERAGE DURATION—PRIMARY CASES

Glands not involved	4.0 mo.
Glands involved	6.6 mo.

The average duration of the cases cured by surgery was 6.5 months, approximately the same as the cases in which the glands were diseased clinically. As practically all of the cases in which the glands were involved died, this implies that the cures were obtained in the tumors of relatively slow growth and low malignancy.

To cure cancer of the mouth it is neces-

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[1] *Surg., Gynec. & Obst.*, 1926, *43*, 377–382. [2] *Ann. Surg.*, 1930, *92*, 681–693.

sary to see the case almost at its inception, that is before the lymphatics are involved. It is even better to destroy a precancerous lesion such as a papilloma or area of leucoplakia, or to remove possible causes of irritation. Metastasis takes place with varying degrees of rapidity, depending on the type of growth and, also, apparently on the situation.

It is unfortunate that cancer at its inception causes no subjective symptoms and the patients do not apply for treatment until the disease is well advanced. Patients with cancer or suspected cancer are seeking advice much earlier at the present time than was the case 10 years ago, due to the publicity which has been given to the disease by the American Society for the Control of Cancer and the various Cancer Clinics that have been established. On the other hand, the gravity of the disease is often not recognized by the first physician consulted, or by the dentist. Thus 30% of 340 cases studied received poor advice from the first physician consulted. In many instances the disease was diagnosed as syphilis or as a simple ulcer and much valuable time was lost in treating the patient for these conditions.

TREAMENT

The treatment of cancer of the oral cavity may be divided into:

(1) Surgery—using the term in the broad sense to include electro-surgical methods, or (2) radiation—either as x-rays or radium, employed as radon seeds, platinum needles, surface application or massive doses of heavily filtered gamma radiation, or (3) some combination of these two methods.

The treatment may also be divided into: (1) The treatment of the original growth, and (2) that of the lymphatic areas.

The actual form of treatment employed is influenced by many things that at first glance have little relation to the subject.

ANATOMY

As has been previously stated, cancer behaves differently in different situations. Cancer of the mouth involves the regional lymphatics of the neck, but very rarely forms remote metastases, or extends beyond the clavicle except in the terminal stages. If the tumor is situated to one side of the midline the glands on that side only are usually involved, although cross metastases do occasionally occur. Without going into anatomical details the chief groups of glands involved, clinically, depending somewhat on the situation of the tumor are:

1. The submental gland.
2. The submaxillary group.
3. The tonsillar gland.
4. Those beneath the upper end of the sternomastoid muscle.
5. Those along the course of the internal jugular vein and intimately associated with it.
6. The glands in the posterior triangle.

PATHOLOGY

Other things being equal, we have found the prognosis depends more on the degree of malignancy as determined by microscopical examination of the tumor than on any other one factor, and this is of great importance in determining the treatment of both the local condition and of the glands.

The following table gives the results of the operations on 100 consecutive cases of cancer, grouped according to the degree of malignancy (Table II).

TABLE II

RESULTS OF OPERATION—PATHOLOGICAL GROUPING

	Cases	Cures	% Cures
Group 1	30	20	66
2	31	11	34
3	24	2	8
4	15	0	0
	100	33	33

In this table the extent of the growth and the type of operation performed have not been considered. The figures imply that tumors of relatively low malignancy are of slow growth and do not form metastases until relatively late in the course of the disease.

Clinically, in certain cases the degree of malignancy can often be recognized. Thus the papillary type of cancer seen more often on the cheek or the alveolar process, and cancer arising in a patch of leucoplakia of long standing are of low malignancy; while the nodular, ulcerated type seen more commonly on the tongue or the floor of the mouth is usually of high malignancy. The lympho-epithelioma of the tonsil is highly malignant but is in a class by itself, and is notably radiosensitive.

The rapidity with which the glands become involved also varies with the situation. This is shown in the following table giving the percentage of cases cured by surgical operations, as practically all cases dying of disease have glandular metastases. Cancer of the tongue and floor of the mouth is seen to be much more malignant than cancer of the cheek or upper jaw (Table III).

TABLE III

RESULTS OF OPERATIVE TREATMENT

Primary cases without Clinical Evidence of Metastases

	Cases	5 Year Cures	% Cures
Tongue	42	12	29
Floor	7	2	30
Cheek	13	6	48
Upper jaw	13	8	58
Lower jaw	14	5	26
Tonsil	2	1	50
Palate	1	1	100
Total	92	35	38

(Operative mortality—1 case in 109 operations .9%)

Besides the above, the extent of the growth and the age and general physical condition of the patient obviously influence the choice of treatment.

DEFINITIONS OF TERMS EMPLOYED

Surgical procedures in the treatment of cancer of the mouth have been standardized for some time, and although there are minor changes in technique, the principle of treating this form of metastasizing cancer has changed but little.

The methods and dosage of radiation treatment, on the other hand, are constantly changing and being improved, and methods approved 5 years ago are not considered appropriate today.

In determining results of treatment, however, it is necessary to study the cases treated 5 years previously, and to wait 5 years to determine the efficacy of the methods in vogue at present.

Radical Operation. Excision of the local growth either with the knife or cautery and removal of the glands of the neck on the adjacent side, together with the sternomastoid muscle and the internal jugular vein from the base of the skull to the clavicle. This operation has been done in two stages at an interval of 10 days. If done in this manner the operative mortality is low, and the deformity much less than would be expected.

Incomplete Operation. Wide local excision of the growth with or without the use of cautery. At present the electro-surgical knife is used in most instances but the actual procedure is, of course, modified to suit the individual case. Excision of the upper or lower jaw is done in the usual manner.

Radiation Treatment. Radium has been used in the treatment of the local growth almost exclusively as seeds of emanation. Since 1923, gold seeds have been used; previously to that, glass. A few cases received surface applications in addition, but I have had no experience with the use of platinum needles of the element. The x-ray has been used in preference to radium in most instances in treating the glands of the neck, as only $1\frac{1}{4}$ gram of radium is available at the Huntington Hospital. It is given at present, since 1923, with the high voltage machine. The patient receives a series of 4 treatments, each treatment being 800 r units, measured in air, at 80 cm. distance, and of approximately 2 hours, duration. Two or more portals are used. When gamma radiation has been used the dosage has varied, but at present the patient receives approximately 32,000 mch. at 10 cm. with 2 mm. of lead filtration. Two portals are used.

In studying the group of cases observed during 1918–24, the amount and form of radiation treatment of the individual cases varied to such a degree that it was necessary to consider each separately and decide arbitrarily whether they had received sufficient or insufficient radiation. In the early cases of the series studied the dosage was distinctly less than that given at present. The figures have not been worked out on the more recent cases, but the impression is that the results following high voltage x-ray treatment are essentially the same as those following treatment with the less powerful machines.

TREATMENT

It is impossible to formulate fixed rules for the treatment of these cases; each must be considered separately, and the treatment that seems best carried out after due consideration of all the factors that influence the prognosis. It is also necessary to determine whether the treatment is given in the hope of permanent cure or whether palliation only is sought.

Cancer of the tongue is a metastasizing form of cancer and it has been the policy to treat suitable cases surgically rather than by radiation, particularly when dealing with the lymphatics of the neck, as at the present time we have no definite proof that all cancer cells when in deeply situated lymph nodes can be destroyed by any form of radiation applied externally. On the other hand, there are relatively few cases that are suitable for radical operation and much harm can be done by ill-advised surgery in advanced cases.

In the series of 763 cases, 227 or (30%) showed no clinical evidence of metastases when first seen at the clinic and radical operation was performed on 48 of these. In other words only 6½% of the total cases applying for treatment were considered suitable for an attempt at cure by radical surgical operation.

If there are obviously cancerous glands present in the neck a radical dissection may disseminate the disease, although this is not always the case if the tumor is of low grade malignancy. On the other hand, many cases have been cured in which no glands were palpable but in which cancer was found on dissecting the neck. A small series of cases was analyzed to determine the significance of small, palpable glands in the neck. It was found that in the cases in which small glands were palpable 45% were not cancer, while in the cases in which no glands were palpable 34% showed cancer on examination of the tissue removed (Table IV).

TABLE IV

METASTATIC GLANDS

Glands palpable clinically (22 cases)		No glands palpable (20 cases)	
Proved cancer	12	Proved cancer	7
Proved not cancer	10	Proved not cancer	13

Although the radical operation if done as described in two stages, in suitable cases, has a relatively low mortality (1 in 48 operations) there are many cases in which it is not indicated on account of the age or general condition of the patient. There is also a group of cases in which the growth is of moderate size without palpable glands in the neck, but of high malignancy in which it is not advisable as it is impossible to obtain a cure by surgical methods in this type of case if metastases have taken place.

TREATMENT OF CASES WITHOUT CLINICAL EVIDENCE OF METASTASES

Local Growth. There is no question that the local growth can be destroyed by several methods. In the early cases we have elected to use surgery rather than radium in most instances, as the operation has little or no mortality and can be done under local anesthesia if necessary. The total discomfort is no greater than that following radium treatment and the deformity much less than is usually supposed. Operation also allows a pathological examination of the tissues to be made. When bone is involved, surgery is always to be preferred to radium as it is difficult to destroy the entire growth with radiation without causing an osteomyelitis which is very painful.

Excision has been done in the past few years with the electro-surgical knife and in certain cases seeds of radium emanation have been implanted in the wound. If the tumor is situated at the base of the tongue the cheek is split if necessary to obtain a satisfactory exposure. Secondary hemorrhage after the employment of electro-surgical methods occurs at times, but can usually be controlled by pressure, although in rare instances it is necessary to ligate the external carotid artery under local anesthesia. Many of these operations recently have been performed under avertin anesthesia, which from the standpoint of the surgeon is very satisfactory, but it is probably not as safe as ether as a routine anesthetic. In certain elderly people, the growth is treated by seeds of radium emanation rather than excision. The bulk of the tumor is estimated and the appropriate number of seeds introduced about the base and edges. This local operation is performed either as the first stage of the radical operation, or in the hope of obtaining a cure in cases without evidence of glandular metastases. We have not advised radiation treatment as a preliminary to surgical excision. In 73 cases without evidence of glandular metastases in which an incomplete operation was performed, that is, excision of the local growth without dissection of the neck, 38% were living without disease five years later, but in all of the cured cases the growth was of low grade malignancy.

Lymphatics of the Neck. In suitable early cases without evidence of glandular metastases a radical neck dissection on one side is advised, but a preliminary course of radiation has not been given because valuable time is lost in so doing. In tumors of high malignancy with small but definitely malignant glands in the neck the operation is not advised as it usually disseminates the growth. Radon seeds are not implanted in the wound, since after a satisfactory radical dissection of the neck there is no place to insert them except in direct contact with the carotid artery or other vital structures. Postoperative prophylactic radiation treatment has not been given as a routine. In the small series of cases in which it was used, in what was considered five years ago to be sufficient amounts, the results were no better than in a similar series of cases which did not receive it. I appreciate the fact that the opinions of many radiologists differ but these are the facts as we have seen them in comparing similar series of cases in which the extent of the disease, degree of malignancy and other factors have been considered.

The radical two stage operation was performed 48 times with 1 death. In 23 instances, the tissues removed from the neck showed cancer. Four of these were cured (17%). In 25 cases the glands showed no evidence of cancer; 34% of these patients were cured. In all of the cured cases the growth was of low malignancy (Table v).

TABLE V
RESULTS—RADICAL TWO STAGE OPERATION

	Cases	% Cures
Glands proved cancer	23	17
No cancer demonstrated in glands	25	34
Operative mortality	1	2

It will be noted that the percentage of cures following radical operation, even if the glands were not involved, is less than that following incomplete operation (Table III). This is due to the fact that there were many cases of very early cancer of low malignancy in the latter group in which it was considered unnecessary to treat the lymphatics. This type of growth is usually seen on the cheek or alveolar process and is papillary in character. If arising on the tongue it is usually associated with a patch of leucoplakia of long standing.

In the large group of cases with a relatively small oral cancer, but in which the physical condition contraindicates radical neck dissection the local growth is excised surgically, although in certain instances it is treated by radium seeds. Glandular areas in this group have been treated by a series of high voltage x-ray treatments, 4 treatments being given and repeated in 3 months. There was no appreciable differ-

ence, however, in the results as far as permanent cure was concerned in the cases that received x-ray treatment and those that did not.

In the highly malignant form of cancer of the tongue, if the tumor is of any appreciable size we are inclined to treat the local growth by excision with implantation of radium seeds, or by implantation of seeds alone after a biopsy, and irradiate the glandular areas of the neck. If metastases have taken place the chance of permanent cure by any method of treatment is remote, and these tumors are at first relatively radiosensitive, but recurrence usually occurs.

The lympho-epithelioma of the tonsil falls in this group and is usually treated by radium seeds after the diagnosis is established with x-ray treatment to the neck. The local growth can at times be entirely controlled by external radiation. Biopsy of any of these tumors to determine the diagnosis and grade of malignancy should be done with considerable care. When performed on an ulcerated growth it is not a dangerous procedure, but removal of a presumably cancerous gland may spread the disease. In the few cases in which this is indicated a skin incision has been made with a knife and the gland excised with the electro-surgical knife.

When the growth is situated at the base of the tongue it is usually advisable to treat the local condition with radium seeds, unless access can be had through a split cheek. A few cases have been excised by a lateral pharyngotomy.

TREATMENT OF CASES WITH OBVIOUSLY CLINICAL METASTASES

This is the most difficult group to treat and, unfortunately, cure is not to be expected. Much can be done, however, to prolong life and temporarily relieve the condition. As a rule it may be said that the cases with obviously cancerous glands are incurable. There are a few cases of cancer of low malignancy with a solitary metastasis that have been cured by operation, but these are the exceptions. This group must not be confused with the group in which small glands are present and in which it is impossible to determine if they are metastatic or hyperplastic. The local condition in this advanced group is usually treated by implantation of seeds of radium emanation, although if it is possible to excise the entire growth this is occasionally done. The glands of the neck are treated by high voltage x-ray, the usual treatment at present being a series of 4 exposures of 800 r units measured in air at 80 cm. distance, each exposure being about 2 hours. It is estimated with a portal of the usual size that with the secondary radiation the tumor receives about 1300 r units. These treatments are repeated about once in 3 months. In certain instances, individual glands are treated by introduction of seeds inserted under a local anesthesia, but no surgical removal of the glands is attempted. More recently in addition to x-ray the patient has also been given a treatment by the gamma rays of radium, the dosage being, roughly, 16,000 mch. at 10 cm., 2 mm. of lead filtration given in one or two positions over the neck. I cannot speak of the results of the cases treated in this manner as they are too few in number and sufficient time has not elapsed since they were treated.

Results. In the series of cases from 1918 to 1924 which have been analyzed the x-ray treatments were usually given by the low voltage x-ray machine or by a radium pack, smaller doses being used than at present. There were 219 cases in this group which had what might be deemed sufficient radiation to accomplish results. All these cases died of disease. Although no permanent cures were obtained life was found to have been distinctly prolonged by the treatment, when the cases were compared with a similar group of cases which had received no treatment. Life was also prolonged by radiation treatment in the cases which recurred after operation.

SUMMARY

It is impossible to lay down any fixed rules for the treatment of oral cancer. Each

case must be considered separately and the appropriate line of procedure determined upon after all of the factors that influence the prognosis have been considered. It is also important to determine at the outset whether the treatment is given with the hope of permanent cure or as a palliative measure.

The local growth can be destroyed either by radiation or by operation, but surgery is to be preferred in the treatment of early cases or cases in which bone is involved.

If the rules advocated by the American College of Surgeons are employed in reporting the results of treatment of cases of oral cancer, it is seen that in suitable cases more cures result by surgical removal than by radiation treatment.

If the growth is highly malignant and of any appreciable size radium treatment is to be advised even if there are no palpable glands in the neck, as this group is radiosensitive and the possibility of surgical cure is remote.

There is also a certain group of cases with considerable infiltration of the floor of the mouth that respond better to radium treatment than to surgical excision.

In the treatment of the local growth by radium gold seeds of emanation have been employed.

The prognosis depends more on the situation of the tumor and the degree of malignancy, as determined by pathological examination, than on any other one factor.

The absence of small palpable glands in the neck does not necessarily mean that the lymphatics are not involved. On the other hand, palpable glands are in many instances hyperplastic and are not necessarily diseased.

Surgery is employed in suitable cases in treatment of the glands of the neck, but much harm may be done by operation if the glands are extensively involved.

In the cases with obvious metastatic glands in the neck, the lymphatics are treated by high voltage x-ray supplemented in certain instances by seeds of radium emanation. Permanent cure is not to be expected but life is considerably prolonged by treatment.

Radiation treatment has not been used as a prophylactic after radical neck dissection as in the small group of cases available for study it apparently did not affect the percentage of cures, in comparing them with a similar group of cases not treated. In cases of recurrence after operation, however, life was considerably prolonged by treatment.

High voltage x-rays are employed in the treatment of the lymphatics as sufficient radium is not available for treatment as a routine measure.*

* For discussion see page 39.

RADIUM AND ROENTGEN-RAY TREATMENT OF CANCER OF THE MOUTH*

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THE radium treatment of intraoral cancer has made great advances during the past ten years not only as to progress in the development of technical procedures but also as to the value and limitations of these agents with special reference to the clinical experience of different sensitivities of tumors to radiation according to the differentiation of their cellular structures.

The monumental work of Quick of the Memorial Hospital, New York, and Regaud, of the Curie Institute of Paris, and their associates, leaves practically nothing to add to the subtle technical procedures which they have evolved. Interstitial irradiation with gold filtered radon "seeds" (0.2 to 0.4 mm.), has been studied experimentally by Failla,[1] Quimby and Martin[2] and Cutler.[3] The clinical application of this experimental data by Quick[4] has shown most gratifying and even spectacular results. He developed a systematic plan of dosage that has been charted within a range of mathematical precision.

Regaud[5] has statistically demonstrated a decided improvement in the end-results of cancer of the cervix by the use of much "harder" or shorter wave-length radiations with 1 to 2 mm. of platinum. Low intensities of radiation are continued over a period of 120 to 240 consecutive hours (5 to 10 days) with total doses ranging from 5,000 to 7,000 milligram-hours with 5 to 6 points of radium. Regaud believes from clinical impressions that there is a particular selectivity of cancer tissue for the very hard gamma rays, and that the results are enhanced by the effect of irradiation during the different stages of mitosis when the cellular selectivity to radiation is theoretically greater. Lacassagne,[6] Canti,[7] and others have also demonstrated this fact microscopically from sections on successive days from actual cases treated with radium. At the Curie Institute these principles of heavy filtrations (1 to 2 mm. of platinum) with small intensities of radiation over a long period of time (5 to 10 days) have been applied to the treatment of intraoral cancer with considerable success. The length of the metal needles of platinum ranges between 15 and 45 mm. and averages 1 milligram of radium for each 15 millimeters of length. Average filtration is 0.5 to 1 mm. of platinum.

The principles of Quick and Regaud have been carried out by many other radiologists with a reasonable duplication of results. Our own experience according to Quick has been most gratifying for the early lesions—involvements technically within the scope of surgical operability—and even in some of the advanced, inoperable lesions, the palliative benefits were sometimes phenomenal.

The insertion of radium needles into cancer tissue is not entirely without danger. The traumatism of tearing small vessels and macerating tissues in a cancer bearing area must not be minimized in the light of possibly setting up an embolic metastasis. The radon "seed" trocar is as large as the average metal needle containing the radium element. There will always be technical difficulties of getting an exact and uniform distribution of the radium "points." When practical all interstitial irradiation procedures at the Philadelphia General Hospital are supplemented with surface or "contact" application of radium in heavily filtered capsules (metal densities equivalent to 2 mm. of platinum), and at the end of about 10 days interstitial irradiation is carried out.

About 60 to 70 per cent of the total dose of both the "contact" and interstitial

* From the Radiological Department of the Philadelphia General Hospital. Read at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, June 8–9, 1931.

routes are employed as compared with an estimated 100 per cent if only one of these procedures were employed. The well known effects of an endarteritis with a generalized fibrosis and obliteration of the finer capillary blood vessels, leucocytic infiltration and hyalinization of tissues argues for the preliminary surface or "contact" applications. A general "congested" state of the tissues will result in ten days, as evidenced by the local radium reaction from surface applications.

When the lesion is very small, superficial or even questionably cancer, it is probably best completely destroyed by electrodesiccation immediately after the diagnostic specimen is taken. At the same time gold radon "seeds" or radium element needles should be inserted into the base and surrounding structures on the basis of a potential cancer. This is usually not sufficient radiation if the average metal needles are employed because the radium element in the needle is usually so far away from the eye of the needle (4 to 8 mm.), that recurrent nodules have frequently been observed to occur at the site of the needle puncture, even with intensities that nearly approached destructive doses. If the biopsy is negative then further radiation is not given. If the biopsy is positive for cancer, then surface applications of radium (gamma rays) must be administered over the primary site of the lesions, in conjunction with external radiation to the glandular region of both sides of the neck. Early lesions about the hard palate, floor of mouth and alveolar processes are generally amenable to surface or "contact" applications. If these regions are treated with interstitial radiation then great caution must be exercised because of the risk of causing bone destruction with the usual complications of pain and infection.

Unfortunately the results of the radiation treatment of advanced, inoperable intraoral cancer is fraught with many disappointments and failures. Statistical computations for these so-called hopeless types of lesions are very confusing and at most do not lend very tangible evidence of any benefits much beyond the province of palliation.

The failure to produce any appreciable permanent effects in the majority of a large group of advanced cancer cases has fostered the conviction that we as radiologists are not administering sufficient radiation.

Even with a noticeable improvement of end-results with the recent development of more accurate technical procedures, these good results for the most part obtain almost entirely for the early or technically operable cases. Technical adjustments have been chiefly an enlightenment on the physical properties of radiation. It seems reasonable that some concerted effort should be made to devise some radical radiation procedure to overcome the deficiencies of treating the very advanced and inoperable lesions.

The wide range of experimental procedures and the wealth of data emanating from these sources has supported many clinical impressions but too often experimental and clinical data are at great variance and sometimes only befog an already muddled situation. The resulting phenomena probably do not change but the interpretations are not uniform and the clinical results do not always harmonize with the conflicting and confusing experimental protocols. This is particularly true when we attempt to analyze these observations with reference to the effect of radiation on tissues. There is a general agreement on the changes as seen in the microscopic picture i.e. leucocytic infiltrations; alteration of cell contour and structure; endarteritis, fibrosis and hyalinization. On the basis of these effects alone technical procedures up to now have been developed.

Short wave-length radiation is one avenue that lends an approach to administering greater intensities than have been ordinarily employed, particularly because these qualities theoretically admit of greater absorption and penetration and certainly

the skin is more tolerant on the basis of clinical observations.

During the past two and a half years, intraoral cancer at the Philadelphia General Hospital has been managed almost entirely with "surface" or "contact" applicators of radium to the primary lesion. This procedure was developed as a means of combating the advanced and inoperable lesions—most of which would ordinarily be classified as "hopeless" and very often would receive only external irradiation to the glandular area of the neck or perhaps be turned away with no treatment except false hopes and sedatives. Some of the advanced cases are ideal for interstitial irradiation alone, but in the majority of instances the extent of involvement would necessitate an intensity of irradiation likely to precipitate a severe local reaction with a resulting condition of misery and suffering that would be hazardous for a weak and toxic individual who is very often feeble not only from disease but from advanced age.

These are the complexities that make up the picture of "hopelessness" and call for the development of some technical procedures that will admit of more treatment and still preserve the physical integrity of the patient.

The universal adoption of 2 mm of brass with supporting physical measurements indicating the quality as gamma rays literally impeded the development of any other technical procedures until Regaud[5] formulated his theory on "hard" or gamma rays (based on clinical and experimental observations). Metal filtrations equal to the density of 2 mm. of platinum, or 2.5 times greater than the density of the usual 2 mm. of brass admit a quality of "hard" gamma radiation which has shown results clinically not comparable by any other technic. Pfahler[8] has also described good results from a wide experience with this quality of heavy filtration.

Theoretically the only biological difference in the varying qualities of rays is one of absorption and penetration. The shorter the wave-length, the greater the penetration and absorption. These are essential factors for the radiation treatment of advanced cancer. The surface tissues will tolerate greater total intensities over a longer period of time than with the "softer" or long wave-length radiation.

Wood,[9] in an experimental study of several thousand animal tumors observed that the lethal effect of the rays was the same whether "hard" or "soft" rays were used. This conclusion argues for a quality of "hard" or short wave-length rays because of its greater penetrative properties.

Lacassagne,[10] in discussing the value of the short wave-length rays, emphasizes the greater tolerance of the skin for the harder rays in addition to their selectivity for cancer and further decries the use of radiation for its caustic benefits, intimating that chemical caustics and electricity are less dangerous and more efficient for caustic purposes since they can be better controlled.

The weight of experimental evidence as well as a preponderance of clinical impressions points to the theory of a direct effect of radiation on cell structure. Since there is no proof, either biologically or physically of a specificity of any particular quality of radiation for cancer and since it has been further shown that the lethal effect is the same for "soft" and for "hard" rays, then the choice of radiation qualities of very short wave-length should be made because they admit of greater depth intensities.

There is still considerable discussion as to whether grading of tumors is practical because of the possible great differences of opinion due to personal equation of evaluating the degree of cellular differentiation. There are other possible complicating factors, i.e. age of patient, location and duration of tumor and local infections. A biopsy from the margin, base or center of the lesion must necessarily modify the cellular characteristics. But all of these difficulties cannot minimize the value that the knowledge of the cellular picture may afford.

Great numbers of cases will eventually outweigh the discrepancies that are certain to develop and after all an approximate average is all that can be expected. It is true that there may be quibbling about the degree of cellular differentiation of a particular specimen but certainly little argument can obtain between a poorly or highly cellular specimen. Whether or not these factors have any bearing on the eventual outcome of radiation treatment must depend upon a careful checkup of the factors of tissue grading, infection, age of patient and duration of the disease, coupled with detailed studies of the final end-results of particular types of irradiation.

TREATMENT OF ADVANCED PRIMARY LESIONS

Inoperable cases have shown clinical regressions with surface or "contact" applications of heavily filtered radium equal to the results obtained with interstitial radiation. In some instances the palliative benefits were more striking. The technic is a conservative means of managing an apparently hopeless case and affords an opportunity of carrying out a fractional dose technic. The great wall thickness of the applicators involves a bulky and almost awkward instrumentation but with a set of stock applicators described by Widmann,[11] the routine treatment of these cases becomes simplified. They are made up speedily and accurately and with little danger to the technician. The planning of a treatment with assistants and nurses is facilitated and a uniformity of technical procedures is developed by an almost automatic routine. The "pegged" arrangement of the capsules for stock applicators is varied with single capsules, or double capsules, in parallel or at the right angles to meet adjustments in the floor of the mouth, dorsum of tongue, against the glosso-pharyngeal fold, the cheek, anterior pillar, the crevices of the upper and lower alveologingival folds and against the palate. Flat applicators with one, two, three or four capsules are easily adjusted against the check, palate and dorsum of tongue.

The use of 2 mm. of platinum admits of wave-length rays more penetrating and less caustic than 0.5 mm. of platinum or its equivalent of 2 mm. of brass, which is the common thickness of filter in general use. For economical reasons the use of lead was selected. These lead capsules can be made to fit any size or number of needles or radon tubes. The radon glass seeds are delivered to us in silver tubes 0.5 mm. thick. The walls of the lead capsules are 3 mm. thick. This thickness of lead and silver approximates the metal density of 2 mm. of platinum. All applicators are covered with pure vulcanizing rubber, 1 mm. thick. The distance from the radium point to the tissues is 5 mm. Because the lead capsules dent and become distorted after long use, they have been duplicated in brass with a wall thickness of 4 mm. to make up an equal density with the lead applicators.

The increased intensity is about two and a half times greater with 2 mm. of platinum than with 2 mm. of brass, and admits of prolonged treatments, following the experience and recommendation of Regaud.[5]

The lead capsules with 3 mm. walls and 0.5 mm. of silver produce an erythema with 350 millicurie-hours in one sitting. If this application is divided over a period of ten days, in amounts of 150 to 200 millicuries, at each sitting, a total dose of 1,000 millicurie-hours can be given. Bachem[12] has estimated a depth dose of approximately 50 per cent at 2 cm. depth, with a surface dose of from five to ten erythema doses with 1.5 mm. of brass.

Ionization measurements are not adequate for determining radiation values with filtrations as great as 2 mm. of platinum. Short wave-length rays admit less scattered and secondary radiation, but the penetration theoretically is greater, and the tissue tolerance extraordinarily greater, so that a total dosage from three ports about a tongue is equal to approximately five erythema doses in the center of the tongue. When this is combined with the external radiation through the neck on both sides,

the total radiation in the tongue will reach six to eight erythema doses. The dorsum and under surface of the tongue will be given approximately 3¼ S.E.D. to each of three areas. The plaque of three and four applicators on the dorsum of the tongue requires 1,500 to 2,000 millicurie-hours because of its larger area. A dose of 1,000 millicurie-hours to each of three areas, right and left floor of the mouth, and dorsum of tongue, gives a total dose from three ports of 3,000 to 4,000 millicurie-hours. If the posterior aspect of the tongue is treated, an additional 1,000 to 2,000 millicurie-hours will be given. It is significant to point out that each "point" area must be treated with divided doses. We average four applications to each area. Lesser filtration with this intensity of radiation is dangerous and will probably produce a radiation necrosis. Frequently a very advanced cheek or tongue lesion requires further treatment and generally an additional 1,000 millicurie-hours is added. This represents the total for a given area, and when the dorsum of the tongue and the floor of the mouth on both sides are treated, a dose of 5,000 to 6,000 millicurie-hours, 0.5 cm. distance, will be attained with additional treatment, which thus far has been used only in very advanced cases.

The local reaction is marked and usually affects all parts about the area treated. The intensity of the reaction is about equal to the local effects about the cheek, roof of mouth, and tongue following interstitial radiation of the tongue with radon (gold seeds). The reaction appears in about two weeks, which is sooner than with the external surface pack radiation, but the total intensity of radiation is much greater.

TECHNIC OF IRRADIATION OF THE NECK

In order to fulfill a program that would permit the delivery of greater quantities of radiation to the tissues, the following procedures have been followed in treatment of the neck:

(a) All ambulatory patients were given high voltage roentgen rays. Two fields—one to each side of the neck extending from the zygomatic process of the face to the base of the neck. Treatments are carried to saturation and usually extended over a period of about two weeks.

(b) All hospital patients were given the advantage of combined qualities of radiation as follows: Two types of radiation were employed on the skin: a combination of roentgen rays, 200 kv., and 0.5 mm. of copper, and radium packs with a filtration of 3 mm. of lead and 0.5 mm. of silver. This amount of lead and silver has a density equivalent to 2 mm. of platinum or gold. It was found that the combination of these two types of radiation, divided over a period of two weeks, permitted 120 per cent of a dose of roentgen rays and 125 per cent of a dose of radium on the same skin area. These factors equal a total of 245 per cent of an erythema with combined radiation to each side of the neck or a total of nearly 500 per cent to both sides, with a resulting depth dose in the middle of the average neck of 2½ skin erythema doses. The erythema is intense and appears in about twenty-one days and lasts about ten days. In certain advanced cases this radiation has been carried out more slowly (saturation technic), and has been extended from four to six weeks. Divided doses over this period of time have permitted as much as 350 per cent of combined (x-ray and radium) radiation to a single skin port without damage. The radium packs are 10×15 cm., with 4 cm., distance. If this pack is given at one sitting the erythema dose is 15,000 millicurie-hours. If divided into four sittings of 48 hours each (5,000 millicuries), a total dose of 20,000 millicurie-hours can be given. Quimby and Pack[13] observed an increased skin tolerance with combinations of different wave-length radiations ("soft" and "hard).

Our routine treatment of intra-oral cancers (hospital patients), therefore, is to plan four radium packs of 48 hours each (total 5,000 millicurie-hours) to each side of the neck, making a total of eight packs, with a total dose of 40,000 millicurie-hours.

This makes a total of 384 hours. On the day of rest between radium treatments a roentgen-ray treatment is given to each side of the neck. A total of six 20 per cent doses is given to each side of the neck. Sometimes radium packs alone are used, and as much as from 50,000 to 60,000 millicurie-hours have been given to both sides of the neck in from six to eight weeks, or 15,000 to 30,000 to a single skin port.

RESULTS

An attempt to evaluate the results of the radiation treatment of advanced intraoral cancer was confined almost entirely to clinical impressions that are obviously only palliative in character.

Ninety-two cases of advanced intraoral cancer were studied. All presented primary lesions technically inoperable. The predetermined plan of irradiation was completed in each instance. Forty-six cases were over 60 years of age; 17 cases were over 70 years, and 2 cases were 80 and 81 years of age.

Of 92 cases 11 were females, and 4 were colored (tongue). Six out of 41 cases showed positive Wasserman reactions.

Of 92 cases, 62 or 67.5 per cent had cervical gland metastasis (21 cases with bilateral involvement). Of these 62 cases, 21 are living 1 to 2 years; 7 of these 21 cases showed complete clinical regression of the palpably enlarged cervical nodes.

Thirty cases with extensive inoperable primary involvement remained free of palpable cervical node enlargement (6 months to 1 year); 11 of these 30 cases died without palpable evidence of enlarged cervical nodes.

Tumor grading did not reveal any definite information except in a few instances; 3 of 27 tongue lesions were graded as type III and clinically did show a more prompt regression.

All lip lesions (21 cases) were graded almost equally as types I and II; the buccal lesions (10 cases) were similarly graded.

Six of 7 palate lesions were graded as type II; only one case was graded as type IV and lived one month after start of treatment.

Four of 18 tonsil lesions graded as type IV showed complete clinical regression. These cases were outstanding illustrations of radiosensitivity. One of these cases developed uncontrollable cervical metastasis within one month after starting treatment (metastasis not palpable at beginning of treatment).

Of 51 living cases, 24 showed complete clinical regression of the primary lesion. Of these 24 cases, 15 involved the lip, 4 tonsil and palate, 3 cheek and 2 tongue.

The greatest obvious palliative benefit obtained in this group of cases has been the effect of irradiation on cervical node metastasis-retardation, partial to complete regression, but more particularly the complete absence of gland involvement in many advanced cases even though the primary lesion was not cured.

As stated above an attempt to set down results on the basis of any statistical computation would only be misleading and confusing. Phenomenal palliative benefits obtain even without apparently increasing the longevity cycle. Regression of the primary lesion as well as the metastatic nodes, diminished pain, general improvement in

	SEX		COLOR		WASSERMANN		DEAD	METASTASIS
LOCATION	M	F	W	C	+	−		
Lip	17	4	21		1	9	6	10
Tongue and floor mouth	27	4	27	4	4	13	20	25
Buccal	10		10		1	3	4	5
Palate	7		7			3	2	4
Tonsil	18	3	21			7	9	18
	79	11	86	4	6	35	41	62

health and strength and even gain of weight with return of appetite and almost normal function of swallowing are criteria that clinically indicate indubitable evidence of improvement.

In the light of our present knowledge, inoperable cancer is essentially a radiological problem. The only other alternative is to do nothing.

While 51 of 92 cases are living, these figures by no means are intended to imply success. The value of this study is an attempt to appraise clinical impressions aside from any theoretical or experimental standard with special reference to the management of an advanced type of cancer of the mouth not readily amenable to the usual procedures that have been successful in the treatment of early or operable intraoral cancer. This experience certainly confirms the observations of Regaud[5] on improved results with "hard" or gamma rays (using metal filters with densities equivalent to 2 mm. of platinum).

If further progress in radiation therapy is to be made then every effort should be strained to devise technics that will permit the administration of greater intensities than are being employed at the present time, and still preserve the integrity of the skin as well as the individual.

The end-results were studied in cooperation with Dr. T. Kapo, radiological student on service at the Philadelphia General Hospital. This assistance is hereby gratefully acknowledged.

SUMMARY

1. Many early cancers have been amenable to a manifold variety of technics in the hands of experienced radiologists.

2. Various treatment procedures are discussed. No adequate technic has been developed to efficiently cope with advanced inoperable cancer.

3. The value of irradiation of advanced intraoral cancer may be defined as largely palliative, and probably dependent upon highly cellular and therefore radiosensitive lesions.

4. Improved results in the radiation treatment of advanced cancer of a resistant type apparently demands a technic and quality of radiation that will permit administration of greater quantities of radiation.

5. The use of additional radiation must depend upon "hard" or short wave-length rays, because of their greater penetrative properties, with a definitely increased skin tolerance.

6. A description is given of stock of applicators for surface or "contact" radium treatments with discussion of technic.

7. Radium filtrations with densities equivalent to 2 mm. of platinum are advocated. This is approximately two and a half times greater than the usual filter of 2 mm. of brass.

8. Results in advanced cases are largely palliative and not amenable to statistical computations.

9. The technic described—"contact" or surface applications (metal densities equal to 2 mm. of platinum)—seems to show improved results on the basis of clinical impressions.*

* For discussion, see page 39.

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THE TREATMENT OF METASTATIC INVOLVEMENT OF THE NECK SECONDARY TO INTRAORAL CANCER*

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BEFORE laying down any special rules for the treatment of malignancy in the cervical lymph nodes, it is well to recall their function. These little collections of lymphoid tissue represent the first line of defense when an infection or any foreign substance gains entrance to the body. If the invader is repulsed, no further progress than the first node is made; however, if not stopped it becomes generalized as a septicemia. Likewise in malignancy when dissemination commences, it is the first lymph node that bears the brunt of the attack. It resists until it is completely filled and its capsule ruptures, when further spread takes place to the next in line. Inasmuch as the node is essentially a filter and since the spread of carcinoma, especially in this locality, seems to be embolic, the progress of carcinoma is hindered by an intact gland. Although there are no studies to corroborate this, it is probable that normal epithelial cells are swept along the lymph stream to the nearest node where they are destroyed, as is the infective organism or a foreign body. The same process takes place in cancer. The defense is perfect as long as the node is not or has not been damaged by a previous pyogenic infection, by syphilis, or tuberculosis. When anatomically perfect and physiologically active, it carries on, but when damaged a foothold is easily gained. It then enlarges; the center becomes necrotic and perforation through its capsule into the surrounding tissues or through the skin takes place gradually.

In analyzing our cases of intraoral malignancy from 1924 to 1930, we find that 520 patients have come for examination or treatment; many of whom were very early cases, but a great number were advanced. When classified we find the following incidence of metastasis to the cervical lymph nodes (Table 1).

TABLE I

	Lip	Cheek and Alveolus	Tongue and Floor of Mouth	Tonsil and Larynx	Total
Nodes at first examination.	22	25	36	36	119
No nodes at any time.	248	54	48	14	364
Developed glands while under treatment.	15	2	7	4	28
Recurrent postoperative nodes	3	1	5	0	9
Total	288	82	96	54	520

A close study shows that less than fifty percent developed metastasis to the nodes during the course of their disease. The incidence was as low as twenty percent in the lip cases and as high as seventy-five percent in the tonsil group. It must not be inferred that all patients that showed no development of metastases got well. An appreciable number succumbed to their primary disease, either as a result of sepsis or because of a sudden massive hemorrhage. Since the rate of metastasis has become more and more apparent to us, it has been our practice to deal with the cervical lymph

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nodes conservatively in the presence of intraoral cancer. This corroborates the work done by Quick at the Memorial Hospital. For this reason patients, as they come in, are placed in one of three groups and dealt with as presented below.

I. *Prophylactic Group.* In this group of patients there is no clinical evidence of malignant disease in the regional lymph nodes. They are subjected to high voltage x-radiation which is pushed to the point of saturation on the side where metastasis may be expected, while on the opposite side only fifty percent of this regular dose is given. Sometimes the question arises as to whether a radium pack should be used; if so, we administer about 6000 milligram-hours, filtered through one millimeter of brass, at three centimeters' distance, over the suspected side. We feel, however, that since the treatment is purely prophylactic it is more economical for the patient if x-radiation is administered, as it eliminates hospitalization. After such a course the individual is kept under close observation and is examined carefully at monthly intervals over a period of one year. If there is no evidence of disease nothing more is done; however, if palpable nodes do appear the patient is treated as in the following group.

II. *Surgical Group.* These individuals have one or more intact, movable, palpable unilateral nodes which are anatomically removable by surgical methods. All such patients are given a thorough course of x-radiation, as in the preceding group, over a period of three or four weeks, and if no perceptible change takes place, two courses remain open—either a resort to radium in the form of a pack or to electro-surgery. Those who, for one reason or another, refuse surgery or who are not good risks because of coexisting disease, are treated with a radium pack at three centimeters' distance, at which time 10,000 milligram-hours are administered. This sets up a severe reaction, and in the radiosensitive types of cell there may be a complete retrogression.

If surgery is decided on, it is done after the edema incident to the x-radiation subsides. The anesthetic is either avertin or ether in oil, administered rectally so that the field is not encroached upon by the anesthetist, and the skin is prepared with five percent mercurochrome in alcohol and acetone. The involved area is then carefully exposed by electro-surgical methods. In some patients the fascia, involved nodes and submaxillary glands are removed in toto, while in others the involved node is isolated and completely destroyed by electrocoagulation. Following this, radium needles containing one milligram of the element and filtered through five-tenths millimeters of platinum, are inserted around the edges of the wound and allowed to remain for about five days; in other cases the wound is closed with drainage and after a week, when closure is assured, a radium pack is placed over the operative tract at three centimeters' distance, giving a dose of about 5000 milligram-hours. In two or three patients on whom this method was tried, and in whom there was fixation to the mandible, a persistent sinus with subsequent exfoliation of dead bone has resulted. This may take from four to six months, but once accomplished the wound heals and there is complete restoration of function.

Another method which we have tried in cases where only a small node is palpable is blind needling with the platinum radium needles. This may be successful but, ordinarily, open exposure and insertion is a safer and more accurate method.

If the deeper chain of nodes is involved and surface irradiation has been carried out, a complete block dissection, as described by Crile, is sometimes done. Undoubtedly many patients are cured by this radical method, but the frequency of local recurrence and the appearance of distant metastasis in individuals apparently well locally, prompts us to believe that in only the very early cases is it successful.

III. *Palliative Group.* Those individuals who come in with massive fixed nodes on one side, or who come in with multiple though movable nodes on both sides of the

neck, are placed in this class. They represent advanced cancer or a very rapidly growing malignant process, and treatment is given with two things in mind.

(a) To retard the progress of the disease.

(b) To relieve pain and prevent rapid breaking down of the masses.

This is accomplished to a certain extent by surface irradiation with minimal doses of x-radiation and by radium packs. The dosage is roughly about fifty percent of an erythema. By this means the patient is saved much discomfort and the necessity of isolation because of sloughing, breaking down nodes which take place after intense irradiation and poorly executed surgical procedures.

DISCUSSION

Surgical textbooks, in dealing with the subject of intraoral cancer and secondaries in the neck, usually dismiss the subject with the advice to do a routine block dissection or a radical dissection of the submaxillary triangle. In our experience this advice seems to indicate that in fifty percent of the cases such surgery would be superfluous. Standardization of treatment is an aim of modern medicine, but certainly in the field of cancer it is necessary to individualize therapy. The fact that a patient with intraoral cancer develops a node does not necessarily mean that it is the seat of malignancy, for undoubtedly some of these nodes are inflammatory. Though we have had no experience with the needling method of doing biopsies, we feel that this will give important information in dealing with suspected enlarged nodes, and if involvement is discovered it will enable the physician to lay out the proper combination of surface and interstitial irradiation after electro-surgical exposure. As time goes on, it seems that one is justified in dealing with the cervical lymph nodes more conservatively than formerly. Proper surface irradiation is advisable, and if this fails one can then fall back on electro-surgical exposure and the use of radium needles. The results seen following this type of management produce less disturbance of function, more comfort, and just as great a degree of life expectancy as with the radical methods.*

* For discussion see page 39.

THE TREATMENT OF MALIGNANT LESIONS OF THE MOUTH BY CONTACT APPLICATIONS OF RADIUM*

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BECAUSE of a somewhat similar appearance and extent of involvement, one is apt to consider epithelioma in the mouth as belonging in the same class with epithelioma of the skin. However, there is a great difference in structure, tendency to metastasize, reaction to radiation and consequently, in prognosis.

A great majority of epitheliomata of the skin, especially if located about the face, are of the basal cell variety. These tumors have a very slow growth, they seldom metastasize, and they are usually quite susceptible to radiation. On the other hand, epidermoid carcinoma of the oral cavity is almost always of the squamous cell type. This lesion, even when occurring on skin surfaces is much more malignant than the basal cell type, it metastasizes early and is extremely resistant to radiation. This lesion is very hard to cure even on cutaneous surfaces where it is easily accessible. It is infinitely more difficult to control in the mouth where, in addition to the customary drawbacks one encounters in malignancy, there are added the complications of heat, moisture and infection, all of which stimulate the growth of the cancerous process. The lymphatic drainage about the mouth is very plentiful and it is seldom one sees a patient for the first time who is suffering from this disease and in whom the cervical lymphatics are not already involved.

For these reasons there is little cause for wonder that the mortality from cancer of the mouth is so high. Even in those cases where by skillful and appropriate treatment the extremely difficult task of eradicating the primary lesion is achieved, the patient still has less than an even chance of surviving his metastases. Since the part allotted to me in this symposium is the consideration of the treatment of the primary lesion by contact applications of radium, I shall not go into any details concerning the treatment of the metastases, although this is usually the more important and difficult part of the treatment.

I have felt for a long time that one of the principal causes of failure in the radiation treatment of malignancy was under dosage. This is often unavoidable because of the nature and location of the involvement, but I believe that many times we under dose a case which is readily accessible because of a failure to realize the amount of radiation necessary to destroy the lesion. The work of Martin, Quimby and Pack[1] in which they show that from seven to ten times an erythema dose delivered to all parts of a cancer is necessary to completely devitalize the tumor should be a lesson to every one practicing radiotherapy. I had arrived at a much similar conclusion many years ago regarding the dosage necessary to cure epithelioma of the face. Since these lesions are almost all basal cell types and quite radiosensitive, it seems probable that squamous cell epithelioma which is known to be highly radioresistant requires even a larger dose for complete eradication.

While there are several other advantages in the use of contact applications of radium in oral cancer, the question of adequate dosage is a very important one since larger doses can be routinely employed with less injurious effects by this method. These larger doses are possible because of the greater filtration which can be employed and also because of the greater distance between the radium and the lesion. The amount of filtration possible in interstitial radiation even if gold or platinum seeds or platinum needles are used, cannot of course be compared with that which may be used

[1] Martin, H. E., Quimby, E. H., and Pack, G. T. Calculations of tissue dosage in radiation therapy (second report). Am. J. Roentgenol. & Rad. Therapy, April, 1931, *25*, 490–506.

* Read at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, Pa., June 8–9, 1931.

in surface applications. This greater filtration results in a higher percentage of gamma radiation which has less escharotic effect per given number of milligram hours than where less filtration is used.

Fig. 1. Various shaped applicators for different locations in the mouth.

In my earliest endeavors to treat cancer of the mouth, a lack of fixation appliances prompted me to use a small amount of filtration in an effort to apply a dose in the shortest possible space of time. The result of this technic was a violent surface reaction, but no appreciable effect on the course of the disease. With improvement in devices to hold the radium in contact with the lesion as long as desired, filtration was gradually added and the length of exposure proportionately increased. Beneficial effects promptly followed this change in technic. In addition to the higher percentage of gamma radiation, another advantage of contact application is the absence of risk of infection which is always present when interstitial radiation is used. This risk was probably greater with the old glass seeds than with gold or platinum seeds because of the area of necrosis which was always present immediately around the seed. The use of radon or radium element inside of platinum needles allows of a greater thickness of wall for filtration purposes and decreases the likelihood of local necrosis. However, since it is impossible to sterilize the field of operation in these cases, there is always a certain danger of carrying infection into the deeper tissues when the radium is inserted. If this happens extensive sloughing may result and this, of course, adds greatly to the patient's discomfort and to his toxemia.

According to Ewing[2] the chief causes of death in cancer of the mouth are pneumonia, septicemia, edema of the glottis and hemorrhage. If the introduction of radium should by chance spread infection and induce sloughing, toxemia would be increased and the danger of hemorrhage become more probable. If too large a quantity of radon is used in each seed, or if the seeds are placed too close together, the danger of sloughing is, of course, much greater. The first factor is easily controlled, but it is not always possible to be certain just what relation individual seeds bear to each other in the depths of the tissues and an error in judgment of this sort may end disastrously. If buried radium or radon is placed too close to bone the periosteum will be destroyed and the complication of necrosis of bone will have to be dealt with. If the treatment has been successful in eradicating the cancer this problem may be met by surgical procedures, but in any event the convalescence will be extremely protracted and distasteful to the patient. I have seen cases of this sort drag on for one or two years after the cancer was destroyed to the intense dissatisfaction of the patient and worriment of the doctor. This complication has not happened to us in any case treated by contact applications.

It is probably true that in the hands of one who spends all his time in treating cases of cancer of the mouth by interstitial radiation many of the untoward complications mentioned may seldom occur. However, the general radiologist who treats the cases of cancer of the mouth as they appear

[2] Ewing, James. Neoplastic Diseases.

in his practice from time to time will, I believe, do better if he adopts contact applications as his routine procedure, reserving interstitial radiation for those cases where contact applications are impossible. I also believe if he is careful that his results will compare favorably with those of the super specialist using interstitial radiation. There are, of course, locations in the mouth in which it is not possible or practical to use contact applications. Areas which are obvious in this respect are the tongue, or in and around the tonsil. If it is not possible to place the radium in contact with the lesion and hold it there for a sufficient period, then interstitial radiation must be resorted to. The length of treatment will, of course, depend on the amount of radium available and the size of the lesion. I do not believe it should be less than 750 milligram hours for each unit of radium applied. Where units are placed side by side allowance must be made for the overlapping effect of each unit on the neighboring area. This dose will have a superficial escharotic effect but will not produce sloughing.

Another advantage of contact applications is that it is not necessary to wait for a considerable period while the mouth is being cleared of infection before beginning treatment. This is usually advisable where interstitial radiation is to be employed, since the danger of introducing infection into the deeper tissues is too great otherwise. The combination of an infected slough plus the original cancer is usually fatal. I hold a little different view regarding cancer and oral sepsis than has been expressed by some authors. It may be that a badly infected mouth may hasten the progress of an existing cancer, but I doubt if it is often an actual causative factor in the absence of some of the commonly known irritative conditions such as sharp teeth, ill fitting dentures, or the use of tobacco. It is true that the average case of cancer of the mouth usually presents a very foul and infected mouth, but I believe this is largely an effect rather than a cause. It is obvious that a patient with such a sore in his mouth cannot carry out the customary processes of cleanliness. Even in those patients whose habits do not include a proper oral hygiene the mouth is usually kept reasonably clean by various hard and rough articles of diet which are necessarily omitted after cancer develops because they would be painful to take into the mouth.

Fig. 2. Applicator in position for lesion in the floor of the mouth.

Where contact applications of radium are employed the treatment can be carried out at once, since the traumatism incident to the application is not great enough to run a risk of spreading infection. As the cancer improves following treatment the infection in the mouth gradually lessens and as a rule when the same period of time has elapsed as would have been necessary to clean up the mouth preparatory to interstitial radiation, the cancer is well on the road to recovery. I believe it is unwise to extract teeth in cancerous areas, or to otherwise traumatize the area of invasion in efforts to clean up the mouth before treatment as the disease may be spread by these efforts. To open up a tooth socket in the midst of a cancerous

lesion seems to me inadvisable and may result in worse complications than the retention of an infected tooth. If offending teeth are not actually in the involved area, they should be extracted as soon as possible

The technic which I have used for some years to hold the radium in position has been previously described before this Society.[3] I still use the same method without any important modifications except that as time goes on I am inclined to use larger doses. Radium element is used in the form of 12½ milligram needles. These needles are placed in brass capsules having a wall 1 millimeter thick and these in turn are placed in rubber tubing. The most common distribution of the radium is in 25 milligram units, although this may be altered to suit the lesion. Thus, if the lesion is a small one and can be covered by one capsule, I commonly use 50 milligrams for this purpose. In larger lesions, 25 milligram capsules are placed side by side, using enough to cover the lesion. Large lesions on the inside of the cheek are sometimes difficult to treat if the patient has all his teeth on that side because there is not room enough for the radium between the teeth and the cheek. Under these circumstances each needle is placed in a separate small brass filter and these are laid in a row and covered with a thin piece of rubber, or two or three layers of adhesive plaster. The radium prepared in the manner described is then fastened on the end of a strip of sheet lead about an inch wide and 6 inches long.

For treating the roof of the mouth, or inside of the cheek, a simple flat strip is all that is necessary. This is covered with adhesive plaster to absorb the secondary radiation from the lead. It is then introduced into the mouth with the radium in contact with the lesion. The portion of the lead strip which projects from the mouth is bent around against the face and fastened there with adhesive plaster and bandages. The lead is sufficiently rigid to hold the radium where it is placed, but of course, is flexible enough that it may be bent into whatever shape is necessary to bring the radium into approximation with the lesion. The bending of the lead strip is, of course, done outside the patient's mouth. Another advantage of using lead for this purpose is that it may be used to protect normal structures from the action of the radium. One side of the radium is naturally against the lead protecting tissues on that side, but if it is necessary the lead may be bent around the edges of the radium also, thus giving protection in more than one direction.

For lesions under, or at the side of the tongue, or on the alveolar process, the lead must be bent into special shapes which will not only hold the radium in position, but will protect surrounding parts as much as possible. These shapes will vary, depending mainly on the extent and location of the lesion and the presence or absence of teeth in the proximity of the lesion. Considerable patience and ingenuity is sometimes necessary to make a satisfactory applicator, but there are few lesions in the locations named which cannot be successfully treated in this manner. If the lesion appears to be of such a nature that an applicator cannot be fitted into it, I make a "trial fitting" so to speak and if unsuccessful in getting accurate approximation, the case is treated by interstitial radiation.

The length of application is usually fifteen hours with 50 milligrams in one unit; sixteen hours with two or three 25 milligram units side by side; and eighteen hours with 12½ milligram units side by side. For convenience the brass filters are usually placed in a section of rubber tubing with walls 2 millimeters thick for secondary filtration. Where it is necessary to have the apparatus as small as possible, two or three thicknesses of adhesive plaster entirely over lead and radium results in smaller bulk and will serve, although I prefer the rubber tubing where possible. I doubt if the filtration value is much different, but believe that the slight extra distance is an

[3] Grier, G. W. Treatment of intraoral carcinoma by contact application of radium. Am. J. Roentgenol. & Rad. Therapy, 1926, *15*, 201–203.

advantage. Such an apparatus in a patient's mouth is naturally far from comfortable and an opiate is usually necessary to make the treatment endurable. Atropine also helps in keeping down the excessive salivation which naturally arises from the presence of this apparatus in the mouth.

As a result of this treatment a radium burn of the first degree ensues. In about ten days the area exposed becomes covered with a thin white slough. Curiously this reaction gives little or no pain. It disappears in from four to six weeks, at which time it is customary to find that the malignant lesion has disappeared also. If the lesion has not healed from this treatment and it is certain that the radium was in accurate contact for the required time, I doubt if a repetition of the treatment will be of any value. If the failure to achieve a cure appears to be due to a displacement of the radium during treatment, or a failure to cover the lesion from other causes, the treatment may be repeated, using a similar technic. However, the object of the treatment is to destroy the lesion in one dose which I believe is the proper policy to adopt in the treatment of any malignant lesion if it is feasible to do so.*

* For discussion, see page 39.

THE USE OF GOLD FILTERED RADON IMPLANTS IN THE TREATMENT OF INTRAORAL CANCER*

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SUCCESSFUL radiation therapy of intraoral cancer requires the use of interstitial irradiation in a large percentage of cases. Since most intraoral growths are highly radioresistant, the tissue dose must be large, and therefore should be confined as much as possible to the tumor and its immediate neighborhood in order to remain within the tolerance of adjacent normal tissues and the organism as a whole. Such a relative concentration of the tissue dose is possible only if the radiating source is placed within the tumor. In practice, it is often of advantage to combine external and interstitial radiation, but physical calculations will demonstrate that the buried source is more efficient and will produce a far greater local effect with a minimum drain on the local and general tolerance.

It will be generally agreed, we believe, that adult intra-oral squamous carcinoma cannot be dealt with successfully by external irradiation alone. We have repeatedly shown[6,7] that such tumors will survive after a tissue dose of about 4 S.E.D. (skin erythema doses) delivered within 10 to 20 days, and we have not found intraoral squamous carcinoma to regress with less than 6 S.E.D. The average range of lethal doses in over 100 measured cases lies between 7 and 10 S.E.D. Anyone familiar with depth doses from external applicators will concede the impossibility of delivering such doses to the midline of the oral cavity by external irradiation alone. Transitional cell carcinoma and certain other anaplastic and radiosensitive growths usually found in the nasopharynx, oral pharynx, and hypopharynx may be successfully dealt with by heavy external irradiation alone. This type of growth is not included in what we term squamous carcinoma in the present discussion.

Interstitial irradiation may be applied either in the form of needles or permanently buried implants. Needles containing either the element or radon are removed after the delivery of a desired quantity of radiation. Seeds are ordinarily permanently buried and, since they contain radon, their dosage depends on their original strength.

Glass seeds (bare tubes) without filter were first devised by Duane,[2] but Janeway[4] and Quick[8] were first to use them extensively. Glass seeds of sufficient strength to be useful in therapy always caused focal necrosis because of the preponderance of the non-penetrating beta radiation which was largely absorbed in the first few millimeters of tissue. This focal necrosis was a distinct disadvantage since multiple focal areas of slough frequently caused a breakdown of the entire mass.

In 1925 Failla[3] designed the gold seed with a filter of 0.2 mm. gold which has since been increased to 0.3 mm. gold. Since 1925, we have not employed the glass seed at Memorial Hospital and at present the gold seed (5 mm. long, 0.75 mm. diameter, 0.3 mm. gold filter) is by far the most widely used form of interstitial irradiation at our institution. It has the advantage of small bulk and sufficient filter to remove 99 per cent of the beta radiation which caused the undesirable necrosis with the glass seed (Fig. 1).

We believe the gold seed to be the most efficient and practical form of applicator for interstitial irradiation in intraoral cancer. Since gold seeds were devised in 1925,

* From the Department of Head and Neck Surgery. Service of Dr. Douglas Quick. Read at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, Pa., June 8–9, 1931.

over 2000 interstitial applications have been given by this means in the Intra-Oral Department. Needles containing the element or radon are preferred in some clinics (The Curie Institute, Radiumhemmet and others), and in some situations will serve as well as seeds. However, a careful consideration of the relative advantages and disadvantages of each, we believe, will demonstrate the superiority of gold seeds for general use. In our department at Memorial Hospital, needles and seeds were used in separate groups of similar cases for over a year. On the basis of comparative results, needles were then discarded in favor of seeds for practically all intra tumoral irradiation.

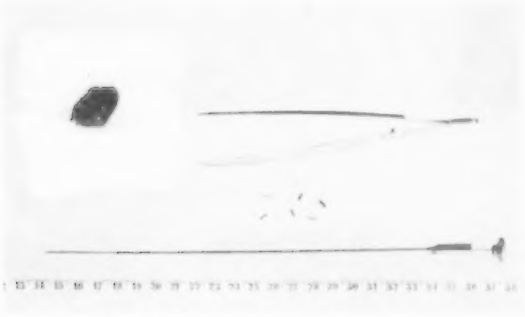

Fig. 1. Gold seeds, trocar needle used for their insertion. The forceps is used in loading the trocar and the tip is then dipped in sterile vaseline to prevent accidental loss of the seed.

Interstitial radiation with element needles requires hospitalization with constant supervision to guard against loss. Therefore the number of patients treated by this means depends not only on the available radium supply, but on bed space, which is quite limited in most clinics. In intraoral cancer particularly, hospitalization is frequently both unnecessary and undesirable, since a considerable percentage of patients prefer to remain ambulatory and even productive during treatment. Bed space may be far better utilized for those requiring operative interference or nursing care. With radon implants, the entire treatment may be given in the out-patient department in the average case. The patient goes

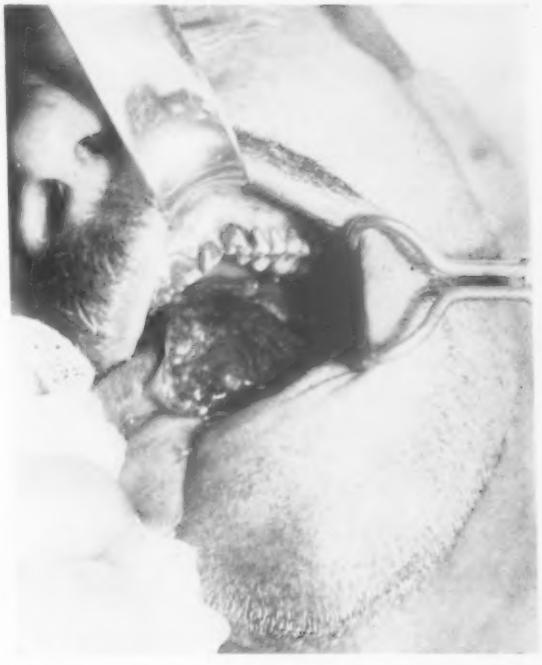

Fig. 2. Case J. D. Carcinoma of the lateral border of the tongue, 5.5×4.0×3.0 cm. in size. "Squamous carcinoma, grade 2, radioresistant."

Fig. 3. Case J. D. The previously involved area two and a half years after treatment with external irradiation and 21.0 mc. of radon in gold seeds.

Fig. 4. Case T. S. Infiltrating carcinoma of the cheek at the angle of the mouth, 4.5 × 4.0 × 1.5 cm in size. "Squamous carcinoma, grade 1, radioresistant."

home immediately after treatment, with an appointment to return in from one to two weeks. All danger of loss is avoided since the implants are of no further value. The patient can be depended upon to return for observation and advice when the reaction occurs.

Needles must have considerable length and bulk, especially if they are to contain such a valuable substance as radium element. The smallest practical element needle is about 1.0 cm. long and 1.0 mm. in diameter to hold about five milligrams or less of element. A smaller or more delicate needle would entail too great a danger of breakage or loss. The comparatively large bulk of such an applicator makes it impractical in many situations where interstitial irradiation is indicated. Lacassagne[5] defines their limitations as follows: "Needles may be correctly implanted only under favorable conditions, i.e., when the tumor is small, easily delimited, and accessible" (Figs. 2 and 3).

Fig. 5. Case T. S. The growth three months after external application of the radium tray and implantation of 32.0 mc. of radon in gold seeds.

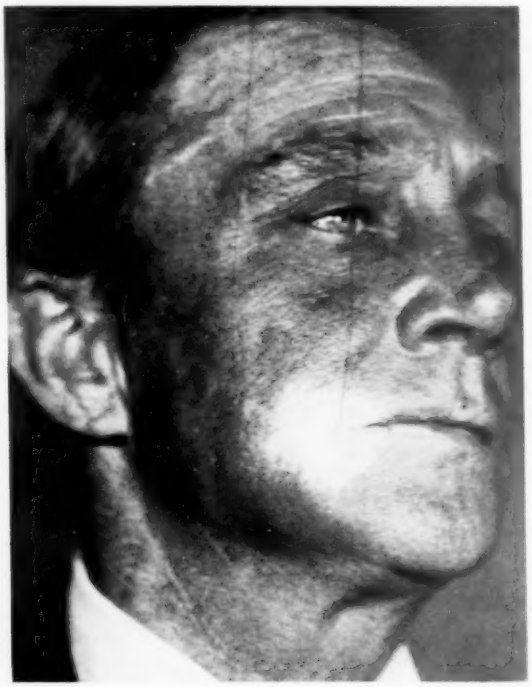

Fig. 6. Case T. S. The skin of the cheek eight months after treatment, with complete healing and no evidence of disease.

The removable radon platinum seed has few definite advantages over the needle. Like the needle, it is removed after the delivery of a predetermined dose, and the continued presence of a foreign body is thus eliminated. Its manufacture is quite complicated, time-consuming and expensive, and its only advantage over the needle is a slightly smaller bulk and the lessened discomfort during its presence in sensitive locations. We feel that it has no definite advantage over the permanently buried gold seed. The removable implant is more expensive, of greater bulk, and requires a more complicated technic for its application. Infection may enter along the course of the attached thread as readily as in the case of the needle. The chances of its dislodgment are considerable since the path of entry is kept open by the attached thread. More trauma is produced by the necessarily larger trocar. The persistence of foreign bodies in the tissues is eliminated by its removal, but we believe this advantage to be more theoretical than practical. The effects of gold seeds as foreign bodies are discussed in more detail below.

Many intraoral lesions are discovered quite early when they may be easily dealt with by one implant in the center. One gold seed may be inserted into or under the center of a small superficial growth, whereas the size of even the smallest needle is out of proportion and it must be more deeply inserted, in order that it may be sutured in place. Since it cannot be inserted as near the center of the lesion, the total dose is less efficient and must be larger. In localities, such as the soft palate and, to a lesser extent the cheeks, superficial but widespread lesions over tissues of little bulk do not furnish an adequate bed for implantation and fixation of needles. The soft palate, if invaded by disease, is very fragile and offers no purchase for holding a needle in position. Seeds, however, may be inserted wth little trauma in tissues of very small bulk and the fragility is of

Fig. 7. Case M. R. Carcinoma of the lateral border of the tongue, 2.0 cm. in diameter. "Squamous carcinoma, grade 1, radioresistant."

Fig. 8. Case M. R. The growth two years after heavy external irradiation and the implantation of 14.0 mc. of radon in gold seeds.

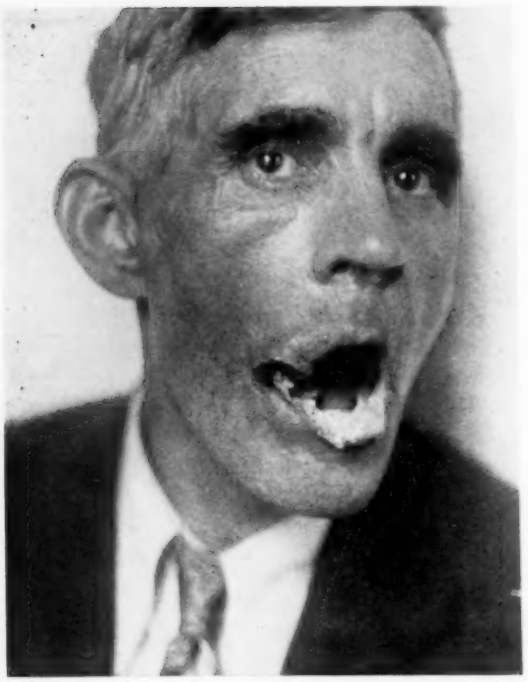

Fig. 9. Case H. J. "Infiltrating squamous carcinoma of the cheek and lips, grade 2, radioresistant."

much less consequence (Figs. 4, 5 and 6).

The difficulty of access to the oral, nasal and hypopharynx almost completely precludes the use of needles in these regions. A trocar containing gold seeds may reach any of these locations either by direct laryngoscopy or through the naris, soft palate, or through the skin of the neck to the base of the tongue, but such approaches do not permit adequate manipulation for the accurate insertion and fixation of needles. In the pharyngeal wall, base of tongue or epiglottis, the extreme functional mobility of the parts makes such bulky applicators intolerable (Figs. 7 and 8).

The common practice with needles as advocated by Regaud and others, is to insert them outside, surrounding and deep to the tumor, which procedure is necessary in order to obtain firm tissue for fixation and suture. This method of placement is extremely inefficient, since at least three quarters of the energy is directed away from the tumor and, therefore, never reaches it. For this reason the total dosage must be larger and as a consequence there is a needlessly severe reaction in adjacent normal tissue as well as a greater chance of slough. We have shown[6,7] from physical investigation that the most efficient method for interstitial irradiation of a spherical mass is from one source at its center. Practical considerations usually make it advisable to subdivide the radiating sources, a principle readily accomplished with gold seeds. Provided that all sources are distributed geometrically about the center, there is little loss of efficiency, if they be kept within the outer third of the radius. These principles, therefore, are more readily carried out with small implants than with needles (Figs. 9 and 10).

The introduction of infection and the occurrence of gross slough is undoubtedly much more common in the use of needles than seeds. Seeds are inserted by a trocar through a surface which can ordinarily be sterilized with iodine. When the trocar is

Fig. 10. Case H. J. Involved area three months after interstitial irradiation with 35.0 mc. of radon in gold seeds. No evidence of disease two years after last treatment.

withdrawn, the puncture wound collapses and chance of infection is slight. The needle is usually not inserted to its full length and infection may enter along its tract during the hours or days of its presence. After its removal the puncture wound does not collapse as readily and the intense local reaction along the needle tract favors local breaking down of tissue extending to the surface.

In our routine treatment of intraoral carcinoma, we use a combination of external and interstitial irradiation. The latter method carries the brunt of the burden and produces a greater part of the tissue dose, except in the highly radiosensitive varieties commonly found in the pharynx where massive doses of external irradiation alone are commonly employed. With permanently buried implants, the intensity of irradiation is greatest at the beginning, diminishing over a period of two weeks to about eight per cent of the original strength. This successive diminution of the intensity may fairly be mentioned as a disadvantage, but it can be overcome only by the use of radium element kept in place for several days at the expense of a great deal of discomfort and danger of dislodgment. It is probable that in practice the principle of prolonged irradiation is as well obtained with seeds as with element needles.

In adult squamous carcinoma we advise a tissue dose* of 7 to 10 S.E.D. Since any departure from the ideal placement of the implants makes the applicator dose† less efficient, we advise the larger tissue dose (10 S.E.D.) in all cases where it seems justified from the standpoint of local and general tolerance. One to two S.E.D. to the midline of the oral cavity or neck may be easily delivered by either x-rays or radium pack and the remaining six to eight S.E.D. given by gold seeds. Since distant external radiation produces a more or less diffuse effect, the applicator dose by this means is not dependent upon the size of the tumor. However, proper dosage by interstitial implantation requires exact calculations for each individual tumor mass. We have already published a table giving quantities

* We have previously defined the tissue dose of a tumor as of that point within it which receives the smallest quantity of energy.

† The "applicator dose" may be defined as a statement of the following physical factors involved during a treatment by irradiation: type of applicator, strength, time, area, distance, filter

TABLE I

MILLICURIES IN GOLD SEEDS REQUIRED TO DELIVER SPECIFIED DOSES TO MASSES OF VARIOUS DIAMETERS

Skin Erythema Doses	Diameter of Mass—Centimeters											
	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	6.0	7.0	8.0
	Number of Millicuries											
1	0.2	0.5	0.8	1.5	2.0	2.4	2.9	3.4	4.0	5.4	7.0	9.0
2	0.4	1.0	1.6	3.0	4.0	4.8	5.8	6.9	8.0	11	14	18
3	0.6	1.5	2.4	4.5	6.0	7.2	8.7	10	12	16	21	27
4	0.8	2.0	3.2	6.0	8.0	9.6	12	14	16	22	28	36
5	1.0	2.5	4.0	7.5	10	12	14	17	20	27	35	45
6	1.2	3.0	4.8	9.0	12	14	17	20	24	32	42	54
7	1.4	3.5	5.6	10	14	17	20	24	28	38	49	63
8	1.6	4.0	6.4	12	16	19	23	27	32	43	56	72
9	1.8	4.5	7.2	14	18	22	26	31	36	49	63	81
10	2.0	5.0	8.0	15	20	24	29	34	40	54	70	90
11	2.2	5.5	8.8	17	22	26	32	37	44	59	77	99
12	2.4	6.0	9.6	18	24	29	35	41	48	65	84	108
13	2.6	6.5	10	20	26	31	38	44	52	70	91	117
14	2.8	7.0	12	21	28	34	41	48	56	76	98	126
15	3.0	7.5	13	23	30	36	44	51	60	81	105	135

Fig. 11. Case J. F. Carcinoma of the dorsum of the tongue 4.0×3.0×3.0 cm., with advanced leucoplakia. "Infiltrating squamous carcinoma, grade 1, radioresistant."

of radon in gold seeds necessary to produce various tissue doses in tumor masses of given sizes. This (Table 1) is used to calculate the applicator dose of gold seeds. From the standpoint of dosage calculation, the average tumor mass is best considered as a sphere or as lying just within a sphere whose diameter is the longest diameter of the tumor. If the tumor is long and narrow or very irregular in shape, it may beconsidered as lying within overlapping or adjacent spheres, each of which is considered separately.

In the average tumor, where several seeds are required, we prefer a strength of about 2 to 2.5 mc. each. Seeds of less than 1.5 mc. in large tumors necessitate undue trauma by multiple punctures, and in some cases, the introduction of too many foreign bodies. If a large tumor mass is used as a holder for radon to irradiate the tumor bed, the entire mass of which is later to be removed, the individual strength of the implants is of little importance. If a superficial circular area is to be treated with seeds in one plane, then one, three, or more seeds should be used. Two seeds cannot be logically used in such a case unless placed together at the center. In spherical masses, one, four, or more seeds should be employed. Two or three seeds, however arranged, will always lie in one plane and are inefficient and illogical for the treatment of a spherical mass.

The implants should be placed within the probable bulk of the tumor mass. Our calculations[7] have shown that a given applicator dose is most efficient if the seeds are geometrically placed about the center within the outer third of the radius. The amount of radon should be kept as small and as efficient as possible since such common complications as slough and delayed healing are in most cases directly proportionate to the applicator dose. Often it is of advantage to insert a precalculated over-

Fig. 12. Case J. F. The tongue four months after treatment with external irradiation and 17.0 mc. of radon in gold seeds. Now free of disease without metastasis.

dose of radon in gold seeds in order that the desired quantity of radiation is delivered within 5 to 10 days at which time the tumor is removed before the height of the radiation reaction. In this way complications following a surgical procedure performed during the intense reaction is obviated, and the immediate postoperative course is less severe (Figs. 11 and 12).

A common objection to the use of permanently buried implants is the supposed later complications, due to the presence of foreign bodies. We feel that the validity of this objection is not greater in comparison to the many advantages of this method of irradiation. Many of the seeds are extruded during the reaction and regression of a superficial process. If buried within deeply seated tumor masses or in neck nodes, the seeds remain permanently without causing any symptom whatever, and the patient is unaware of their presence. Such a case is illustrated in Figures 13 and 14 where seeds were implanted 5 years ago. This patient is free of disease and symptoms of discomfort, although a recent roentgenogram demonstrates the presence of several gold seeds at the site of the primary lesion and a former metastatic node over the carotid bulb. Figures 15 and 16 show the present condition of a patient with cancer of the anterior third of the tongue treated over two years ago by a combination of external and interstitial irradiation. Thirty millicuries in gold seeds were inserted into the tongue. During the following six months, four separate metastases developed in the neck, three on the left and one on the right. These were individually exposed and implanted with gold seeds. Figure 17 is a recent roentgenogram demonstrating the presence of gold seeds as foreign bodies in the cervical nodes and in the tongue. They are causing no symptoms and the condition of the skin of the neck and of the tissues of the tongue is satisfactory. After healing has taken place, we have not observed any symptoms of discomfort that could in any way be attributed to the presence of foreign bodies. The only valid objection to their presence

Fig. 13. Squamous carcinoma of the floor of the mouth with one cervical metastasis over the carotid treated in June, 1926, by the implantation of nine gold seeds containing 20.0 mc. of radon in the primary growth and six gold seeds containing 10.0 mc. in the metastasis. This photograph shows the patient five years after treatment free from disease and from symptoms.

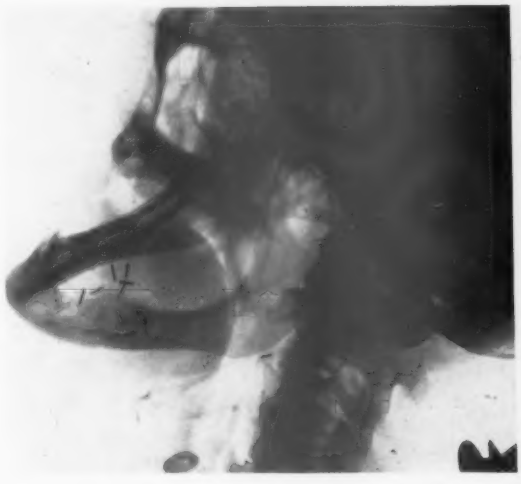

Fig. 14. Same case as shown in Figure 13. The roentgenogram shows the gold seeds in place after five years in both locations of the primary and metastatic carcinoma.

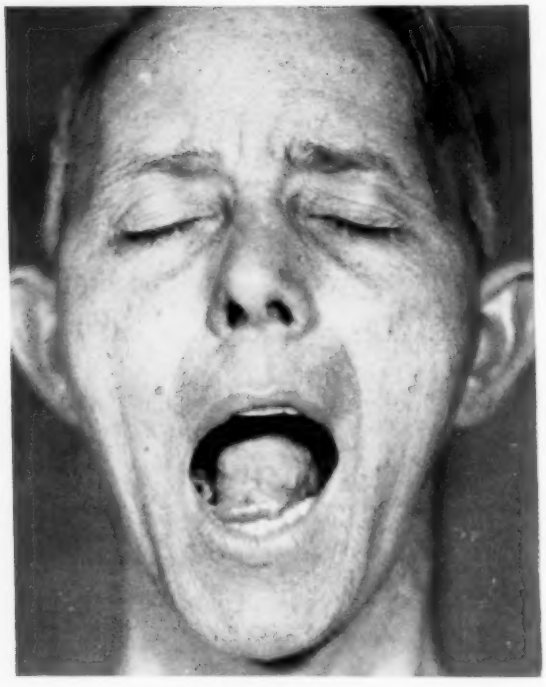

Fig. 15. Case R. J. Carcinoma of the tongue treated over two years ago by insertion of 30 mc. in gold seeds. The patient is free of disease and the function of the tongue is quite satisfactory.

might be a greater tendency toward late necrosis in heavily irradiated tissue. This does occasionally occur, but it also may follow heavy irradiation by any method. Late necrosis of skin is commonly observed after heavy external irradiation. We believe that the immediate probability of necrosis is lessened by the avoidance of deep infection which it must be admitted is favored by the incomplete insertion of a needle or the presence of an attached thread.

Careful attention must be given to the proper placement of seeds at the time of their insertion. Haphazard placement, without regard to the geometrical distribution, will account for many failures. Most cases are treated without admission to the hospital for implantation of the seeds. If the lesion is superficial, the insertion of seeds may be carried out after application of 10 per cent cocaine solution to the mucous membrane. The area through which the punctures are made should be sterilized by tincture of iodine.

In other instances of larger and deeply infiltrating lesions, conduction anesthesia permits more leisurely, careful, and painless manipulation. The anterior half of tongue, floor of mouth, alveolar ridge, and lower lip may be readily anesthetized by an inferior dental block such as is commonly used by dentists. The tip of the index finger is placed on the occlusal surfaces of the lower molars and with the dental syringe 5.0–6.0 cc. of 1% novocaine are injected into the tissues mesial to the retromolar trigone along the inner surface of the ascending ramus to a depth of about 2.0 cm. Such an injection will anesthetize the lingual and inferior dental nerves. It is not practical to attempt the blocking of one nerve alone, since the position of the lingual nerve is variable and it is always anesthetized by the above procedure along with the inferior dental nerve. If the lesion involves the posterior half of the tongue, blocking of the lingual nerve will not suffice and in such a case field block of the base of the tongue

Fig. 16. Case R. J. Showing skin of neck two years after surgical exposure and implantation of gold seeds in two metastatic nodes.

may be performed through the neck above the hyoid bone. In the cooperative patient, insertion of the seeds may be accomplished quickly, although not without some pain, by a surface application of 10 per cent cocaine. Short general anesthesia is indicated when technically difficult and painful implantations are required in apprehensive patients. Tumors of the base of the tongue in the region of the epiglottis are best implanted through a stab wound in the midline of the neck just above the hyoid bone. With a palpating finger in the mouth the placement can be quite accurately controlled.

In the treatment of cervical metastasis from intraoral carcinoma, we are more and more dispensing with neck dissections in favor of implantation of the separate nodes by gold seeds. After several years of experience with block dissections of the neck, we believe that implantation with gold seeds offers equally good end-results in operable cases, without the operative risk of the major surgical procedure. (Figs. 13 and 14). Inoperability from the standpoint of complete removal does not preclude surgical exposure and implantation of nodes by radon seeds. Our success with the latter type of metastases led us to extend this more conservative method of treatment to operable nodes formerly dealt with by block dissection. Quick[9] has published in detail our technique for this method of treatment of metastasis. If a metastatic node is small (1 cm. or less) and superficial, implantation may be done through a very short stab wound in the skin. In such cases it is preferable to use a single implant which may be as strong as 3–4 millicuries if necessary. There is no danger of superficial necrosis if a seed of this strength is buried at least 1 cm. below the skin surface. Larger nodes and those at a greater depth, require surgical exposure. The incision need only be long enough to expose the outer surface of the node so as to permit its accurate localization and measurement. The number of seeds and their total strength is then selected to deliver the desired tissue dose.

Fig. 17. Case R. J. Roentgenogram of case of carcinoma of the tongue shown in Figures 15 and 16. Groups of seeds are seen still in place in the tongue and in four separate nodes of the neck.

Widely separated metastases are exposed through independent short incisions.

Irradiation will not always bring about the regression and absorption of large liquefied or necrotic metastatic nodes. Persistent draining sinuses are a common complication even after adequate irradiation. Such nodes may be implanted directly through the skin and surgically removed or curetted after the delivery of an adequate tissue dose. A variation in technic in exposure, removal or curettage and the implantation of seeds into the base of the wound which is then packed wide open with gauze to heal by granulation.

Massive metastases (4–6 cm.) require correspondingly large applicator doses of seeds. Convalescence is often made easier if such masses are excised a week to 10 days after implantation, thus obviating the necessity for the absorption of a large mass of condemned and devitalized tissue.

Such a flexible technic as the one out-

lined above cannot be carried out with either needles or removable seeds. Deeply situated nodes would necessitate reopening of the surgical incision for the removal of either needles or seeds. Such a secondary surgical procedure enormously increases the danger of infection and slough. In the neighborhood of large blood vessels or other important structures, the prolonged presence of several such bulky applicators as needles would be attended by considerable risk of trauma. One of the greatest disadvantages in the use of either radon or element needles is their comparatively high unit content, which does not permit the smaller subdivision of radiating sources and proper distribution. This together with their unwieldy bulk prohibits a sufficiently flexible technic to meet the requirements demanded of the various conditions such as size, shape, nature, and location of cervical metastases.

Comparatively large quantities of radium (at least 0.5 gm.) in solution, an emanation plant and various other costly appliances are required for the efficient production of radon in any form of applicator. Except by purchase from commercial firms, gold implants are, therefore, unavailable to individuals possessing limited quantities of radium. For intraoral purposes such limited amounts are most efficient if confined in a number of needles of the smallest practicable size contianing 1–5 mgm. each. The technic and physical principles employed in the use of gold implants could more nearly be duplicated by these small needles than by any other form of applicator.

The principles outlined in this paper are applicable to growths in any part of the body wherever interstitial irradiation is required and we believe that with few exceptions the gold seed is the most generally useful form of intra tumoral applicator.

SUMMARY

Successful radiation therapy of intraoral cancer requires the use of interstitial irradiation in a large percentage of cases. The relative merits of gold radon seeds, removable platinum radon seeds, element and radon needles are discussed. The technique of interstitial therapy by gold seeds in intraoral cancer and neck metastases is described. Permanently buried gold radon implants are the most efficient and generally useful form of intra tumoral applicator.

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DISCUSSION OF PAPERS BY DRS. STEWART, SIMMONS, WIDMANN, MELAND, GRIER, AND MARTIN AND SHARP

Dr. George E. Pfahler, Philadelphia. I have been especially interested in the treatment of cancer of the mouth by irradiation, and I would like to express my personal appreciation of the excellent papers which have been presented and to Dr. Quick for arranging this symposium. In the introduction of Dr. Stewart's paper he has given us the difficulties involved in determining the radiosensitivity in any particular case of cancer of the mouth. As he has well said, there is a variation according to the location from which the biopsy has been taken. Therefore, one must utilize considerable experience or clinical judgment in the removal of the specimen. Dr. Bothe has recently described a case of carcinoma in which the four grades of malignancy were shown in different sections of the same tumor. The failures described by Dr. Stewart occurred from insufficient irradiation applied to the lymphatic areas, especially on the opposite side of the neck from the location of the primary lesion. I believe it is wise to use nearly as much irradiation on the opposite side as on the affected side. Clinical observations, even independent of the typing of the tumors, has shown those occurring in the pharynx, soft palate and the tonsils to be especially sensitive to irradiation. In general, I believe it is wise to carry our irradiation to the limit of normal tissue toleration, rather than to aim at the minimum irradiation which might be necessary.

Every case of cancer of the mouth must be considered individually and not treated according to any rule, for cancer does not follow any rule in its development. Like Dr. Grier, I have become enthusiastic in the treatment of cancer of the mouth by surface applications with highly filtered radium. We must all agree with Dr. Grier that the treatment of the lymphatics is most important, and I also agree that most failures occur because of under-dosage. To avoid the infection, whenever possible the interstitial irradiation should be used through the skin instead of through the mucous membrane. Traumatism should be avoided as much as possible. The lead clamp method of applying the radium which was described by Dr. Grier is most valuable. It permits much individualization, and is less bulky than the use of the dental compound. I would also like to emphasize the importance of making the treatment thorough from the beginning.

It is a great satisfaction to hear that Dr. Widmann has continued the technique at the Philadelphia General Hospital which we developed in my private clinic which consists (1) of prolonged surface irradiation to the limit of normal tissue tolerance almost constantly during a period of three weeks; (2) of using highly filtered gamma rays through 1, or better, 2 mm. of platinum, and (3) of supplementing when necessary with interstitial or roentgen irradiation.

Drs. Martin and Sharp are to be congratulated upon their clear and practical presenta tion of their subject. They certainly are correct in the statement that one cannot depend upon external irradiation alone in overcoming cancer of the mouth. A great gain has been made in the use of interstitial irradiation since the glass seeds have been replaced by more highly filtered containers, either by the use of gold or platinum implants as devised by Failla, or the use of iridium-platinum needles containing the radium element. I have used almost entirely the radium element. The increased filtration by 0.3 to 0.5 mm. walls has undoubtedly given better results. The danger from cancer is its growing edge, and I believe that it is more important to insert radium about this border or in the outer third of the radius rather than into the center of the tumor. When possible the needles should be inserted through the skin. This almost eliminates the danger of infection.

Dr. Simmons' excellent paper contains so much valuable material that it is difficult to do justice in discussion. Two sentences, however, contain the gist of successful treatment of cancer of the mouth: "*To cure cancer of the mouth it is necessary to see the case almost at its inception, that is, before the lymphatics are involved. It is even better to destroy a precancerous lesion such as papilloma or area of leukoplakia, or to remove possible causes of irritation.*" If we could only keep this motto continually blazing before the public and the profession, the greatest good would be accomplished.

The fact that only "6.5 per cent of the total cases applying for treatment were considered suitable for an attempt at cure by radical surgical operation" is proof enough that we cannot depend upon surgery alone as a satisfactory means of treating cancer of the mouth. I am thoroughly convinced that the radium packs

applied as I have previously described are far superior to any form of roentgen treatment in cancer of the mouth. I have never had satisfactory results with any form of roentgen rays. I am, however, very much more enthusiastic concerning the use of radium in the treatment of cancer of the mouth, particularly by the use of pure gamma radiation highly filtered. We still lack the long period of observation demanded by Dr. Simmons, but we all know that in the great majority of cases, recurrences, if they do occur, will develop within the first year. I am also convinced that the more cancer we can cure without operation, the more will come to the physician in an early stage.

Dr. Meland has hit the nail on the head when he said, "In the field of cancer it is necessary to individualize therapy." The radiologist who can best survey the history, extent of the disease, and the general conditions of the patient and then adapt the therapy best suited to the individual will accomplish the best results. This excellent symposium which has been so will planned by Dr. Quick gives to us some general guiding principles and information but, after all, the man who has cancer must be treated as an individual. When dealing with palpable lymph nodes, one can only be certain that they are or are not malignant by surgical dissection and microscopical examination. When they are firmly adherent and infiltrating they are malignant. My attempts at needle biopsies on movable glands have been failures. I would rather depend upon my clinical judgment. However, if we get rid of the lymph nodes we will have accomplished the desired results so far as the patient is concerned. It is our practice, as previously described, to irradiate the lymphatic areas in all cancers of the mouth with radium packs at 4 cm. distance with a filtration of 1 mm. platinum and 1 mm. gold to the limit of normal tissue tolerance which is usually from 18,000 to 24,000 milligram-hours and often supplement this with local insertion of radium needles, preferably with 2 mg. needles in 0.5 mm. of platinum for about five days. This has given us more satisfaction than surgical dissection.

Dr. Wm. Neill, Jr., Baltimore, Md. As a result of the papers presented I am sure we shall all return home with renewed interest, with the ideas gleaned in the diagnosis, classification and treatment.

As in malignancy in general, I feel it is impossible to lay down precise rules covering the radiation treatment of the various forms and extensions of intraoral cancer; each patient must be studied separately, and greater dosages given the advanced than the early cases.

The treatment of intraoral cancer has undergone radical changes during the past ten years with the advent of radiation. Our present position is that in early, well-localized, accessible lingual growths without extensions onto the floor of the mouth and without glandular metastasis, complete removal with the electro-cautery is preferable. This also affords an opportunity to make a pathological study and becomes as well a guide in any subsequent irradiation. Low-grade, warty epitheliomata as a rule are curable in this way, while the more malignant grades III and IV are apt to metastasize, regardless of the size of the lesion or the duration of the symptoms. It is advisable here to irradiate the neck to the skin tolerance, which can be done with roentgen radiation or large amounts of gamma radium through multiple skin portals.

In the more extensive lesions, with involvement of the floor of the mouth or adjacent structures, the best treatment is by radium alone or combined with roentgen rays. Here we use a flat topical application together with the implantation of gold radon segments. When situated far back on the base of the tongue, stronger permanent implants are preferable as yielding a more accurate radiation. Great care must be exercised not to make the interstitial application too close to bone, producing painful periostitis followed by necrosis. We use strong radon points, from 5 to 10 mc. each, without any resultant severe reaction or sloughing; these are implanted under direct vision, with local anesthesia, using the finger as a guide. For a flat application we use a tube or combination of tubes attached to a suitable applicator, held by the hand and under constant vision, retracting the adjacent normal tissues meanwhile away from the radium. When these large amounts of radium are used in topical applications the operator stands behind a thick lead screen. In more advanced and hopeless cases, a preliminary ligation of the lingual or external carotid artery is often advisable. Hygiene of the mouth is important to obviate a secondary invasion by Vincent's and other pathogenic organisms. The question of nourishment is at times exceedingly important, when, if neces-

sary, the feeding is by the nasal tube or a preliminary gastrostomy.

Cheek, tonsillar, roof of mouth and pharyngeal wall lesions are treated locally along similar lines.

In the early cases with no palpable glands, with a patient available for frequent observation, we feel it safe to wait and watch. Where only one or two small and freely movable glands are felt, surgical removal of the upper anterior and posterior group may be advocated, followed in a few days by postoperative external roentgen or radium irradiation, as outlined.

For fixed, extensive metastatic gland masses, the implantation of large gold points and heavy external irradiation over multiple portals is preferable. Under this treatment we see large masses completely disappear. We do not advocate a skin incision in order to place the radium tubes under the flaps, nor yet do we recommend destruction by any type of cautery or electrosurgical procedure.

Dr. Fielding O. Lewis, Philadelphia (by invitation). I greatly appreciate the honor of being invited to discuss this very interesting and instructive symposium. I am not a radiologist, but from the standpoint of a laryngologist, I have for several years been deeply interested in oral cancer. From my own experience, in the treatment of intraoral cancer, in cooperation with Dr. Widmann of the Philadelphia General Hospital and others, and from what I have heard today, it seems to me that as yet no fixed rules for treatment are applicable to all cases. I am, however, convinced that for the proper treatment of this very grave disease, there are certain necessary essentials, two of which I deem most important: (1) a careful history and complete study of the patient, noting site and extension of the lesion; (2) congenial cooperation between a competent radiologist, and accomplished pathologist, and a skillful surgeon, not to mention an adequate amount of radium.

It is interesting to note that Dr. Simmons has found in his large series of cases, a greater percentage of five-year cures following surgical procedures than by irradiation, which would indicate perhaps that non-surgical methods in intraoral cancer are considered by some to be of secondary importance.

With improved technique in the permancefor of lateral, translingual and subhyoid pharyngotomy, better results and lasting freedom from disease are being accomplished.

In my own experience in the treatment of cancer of the epiglottis, base of the tongue, pyriform sinus, and the hypopharynx, the use of electro-surgical methods, when possible, followed by irradiation, have been by far the most satisfactory. If irradiation precedes an extensive surgical operation, serious difficulties are encountered, incident to fibrosis. On the other hand, in the treatment of cancer of the tonsils, soft palate and tumors of the nasopharynx, the surface application combined with interstitial applications of radium is, in my opinion, the method of choice.

All methods have been tried in the treatment of metastatic glands of the neck, including surgery, electro-surgery, and implantation of radon tubes, but our best results have been obtained by high voltage roentgen treatment.

Dr. Arthur C. Heublein, Hartford, Conn. My experience in using contact radiation in treating the intraoral group of malignant diseases is largely confined to accessible tumors such as the floor of the mouth, the alveolar process and the anterior buccal mucous membrane. The application is usually made by imbedding radon tubes in dental compound after a preliminary impression of the lesion has been taken. It seems to me its use in the intraoral group is distinctly limited but that it may have certain advantages as a preliminary step before interstitial radiation is used in order to inactivate cancer cells before implanting the lesion, and in selected cases such as the alveolar process where there is a danger of bone necrosis if gold implants are used. As pointed out by Drs. Martin and Sharp, the use of platinum needles is limited to accessible fields, the danger of infection being greater and the procedure more complicated than in using gold implants. Too many cases have been successfully treated with permanent gold implants to warrant criticism of this method on the basis that foreign bodies are being retained which will later produce serious untoward effects. There may be some advantage, however, in obtaining more uniform prolonged irradiation effects in the use of platinum needles as compared to the gold implants. I have had no experience with the heavily filtered contact applicators as described by Dr. Widmann and Dr. Grier.

The classification of tumors by the pathologist in the intraoral group according to their

degree of radiosensitivity has been of real value to the radiologist in determining dosage. However, as Dr. Stewart has pointed out, one should not limit the amount of radiation delivered because a tumor is thus classified but in order to strive for the highest percentage of arrest, the dosage should be limited only by skin, tissue and general physical tolerance of the patient.

In treating the highly malignant radiosensitive group of cases such as the transitional cell carcinomas and lymphoepitheliomas which so frequently yield brilliant local results, we are often disappointed in the subsequent course of the disease. In spite of our best efforts, the end-result is usually death due to rapid development of distant uncontrollable metastases. Wide dissemination of the disease may be present but unrecognized at the very time we are treating local lesions. As we all know the adult radioresistant group of carcinomas yield by far the best end-results for they tend to remain localized and it seems that the present methods employed are satisfactory. In the main, we may feel justly proud of what we, as radiologists, have accomplished in controlling this latter group.

It has been increasingly evident to me that there are certain ideals in applying external radiation therapy, the realization of which has never been fully accomplished because they have never been satisfactorily combined:

I. Uniform distribution of the radiation throughout the tissue undergoing treatment.
II. Constant irradiation to affect those cells undergoing mitosis.
III. Irradiation of the entire body in the hope of controlling distant unrecognized metastases.

During the past few years it has been my desire to constantly irradiate the entire body over a prolonged period of time with a target-skin distance measured in meters rather than centimeters. Such a delivery throughout the tissues of a more uniform, more nearly homogeneous quality can be produced by increasing target-skin distance and filtration.

We have recently accomplished almost constant irradiation by using a specially designed automatic machine which permits the continuous operation of a roentgen tube day and night except for such time as is required for the necessary nursing care of the patient. The only hope of controlling distant metastases by irradiation methods before they become clinically evident seems to be in irradiating the patient's entire body. Of course this may give indirect, possibly constitutional, as well as direct radiation effects. Can the entire body tolerate such a procedure? This can only be determined by a careful survey of the reaction of the body as a whole and a gradual building up of dosage. Therefore, it would seem that combining the three procedures formerly noted might lead to improvement in end-results, particularly in the radiosensitive carcinomas, the lymphomatous group and in the blood dyscrasias.

We are now carrying on certain clinical experiments at the Memorial Hospital, New York City, embracing these principles to their fullest practical extent. These experiments are being conducted by a group of specialists in order to consider these methods from all angles—medical, pathological, physical and radiological. An automatic apparatus has been installed which is now in operation irradiating patients in the manner previously noted. A description of the set-up will be published shortly.

Dr. Henry K. Pancoast, Philadelphia. When we consider the details of the various procedures advocated there are almost as many methods of treatment suggested as there have been essayists, although the general principles involved are quite similar in most instances.

There are certain outstanding features of mouth cancer which have been well stressed and which must be given due consideration in order to deal successfully with the disease. The most important of these is the very nature of the growth, which is usually of the squamous cell type and highly resistant to irradiation and which metastasizes readily and rather rapidly. It tends to infiltrate deeply and often into inaccessible localities. There is always the constant annoyance of infection which is impossible to eliminate entirely and which may be responsible for serious complications. Finally, there results from the treatment an interference with the function of the oral cavity as a part of the digestive tract which may seriously imperil the patient. This may be the result of pain, interference with mastication, crippling of the swallowing mechanism or loss of appetite.

The nature of the growth and its location make surgical procedures of the excision type undesirable in most instances. The success of non-surgical measures, including electrodesic-

cation, in so many cases as compared to that obtained by surgery in connection with the primary growth, has transferred mouth cancer largely into the list of radiological conditions, as has been the case with uterine cervical cancer.

We can all agree that radiological measures have not yet reached their greatest possible perfection in technique, and it behooves us to use every possible means to improve our methods in order to obtain the best results. There has been a wide variety of methods employed during the development of radiological technique for the treatment of intraoral cancer. In the earlier years of the use of radium the treatment was often ineffectual because of the lack of adequate filtration, which resulted in painful superficial sloughing and insufficient depth dosage. The latter shortcoming was partially overcome later on by needle and radon seed implantation. This Society, in the comparatively short period of time since its inception, has seen remarkable strides in the development of the technique of radium applications. It seems but a very few years since one of the charter members and former presidents, the late Dr. Lee, showed you a simple device for the fixation of radium containers used for surface applications within the mouth. Grier has many times demonstrated similar devices. These are still in use. The dental compound fixation method has almost gone into the discard except in the treatment of the more superficial growths.

The greatest evils and deficiencies of the early methods have been largely corrected by the use of highly filtering radium containers which provide for a far greater depth dose with less superficial sloughing and far less discomfort.

It is now generally agreed that the first procedure in treating mouth cancers is the surface application of as large a dose of highly filtered radium as is advisable. Grier did not mention it, but he probably intended to do so, that this must be reinforced by external irradiation by high voltage roentgen rays or highly filtered radium packs or both. We employ, for the internal surface applications, 2 mm. brass containers for a dosage of 150 to 200 mg-hr. to the appropriate area of distribution of the unit of 50 mg., or 450 mg-hr. with the use of 3 mm. lead containers. It is evident from what we have heard of the radiosensitivity of mouth cancer, or, more correctly speaking, its radioresistance, that these measures will be effectual in only the more sensitive growths. Additional radiation can be applied only by interstitial irradiation by implanted needles or radon seeds.

Electrodesiccation methods were largely in vogue for many years and were widely heralded even by those who have now almost discarded them. I am not one who advocated throwing these methods entirely into the discard. I have been unable to repeat by irradiation alone, even by the most modern methods, some of the results obtained six, eight and ten years ago by the widely destructive effect obtained by electrodesiccation. The supposedly terribly crippling scars so produced will loosen up in time. We practically dropped this method of treatment for a time, but we are again going back to it in many cases, especially in dealing with growths in the region of the lower alveolar-ramus angle which tend to infiltrate backward into the pterygomaxillary fossa, many growths of the superior maxilla, especially when invading the maxillary sinus, through and through infiltrations of the cheek and in lower alveolar bone involvement. There is a limit to the ability of depth dosage to reach some of these growths adequately and for implants to be made safely and satisfactorily, and accessibility by destructive electrodesiccation is often a great advantage. We must always bear in mind that in treating mouth cancer each growth may be a law unto itself and no hard and fast rule is applicable to every case.

The tongue is one part of the mouth in which it is extremely difficult to satisfactorily make applications of highly filtered surface radium applications. Electrodesiccation is not desirable in most instances. Radon implants are used in this locality more frequently as a routine procedure than elsewhere in the oral cavity. A repetition of interstitial irradiation is likely to be followed by late sloughing as a result of endarteritis, but we have never regarded this means of ridding the patient of a suspicious area of tissue as a great detriment, even though it may be uncomfortable and annoying.

Grier is correct in stating that our first results should be the favorable or desired ones in most instances. Repeated irradiation of the normal cellular components of a growth area makes a favorable soil for recurrence and rapid spread.

The lymph node areas in all oral cancer cases are either metastatically involved or must be regarded as potentially the seat of metastases. The lymph channels and nodal regions of every

case must be carefully treated, whether involved or not. To do otherwise is to shirk a great responsibility. Most of us probably do not treat the apparently uninvolved cases as energetically as we should until an obvious nodule appears. Theoretically, at least, uninvolved gland areas should receive a heavy dose of high voltage roentgen rays which may be reinforced by a radium pack. If properly applied, such treatment is efficacious. Certainly to us routine block dissections seem superfluous, as Meland states.

In cases with involved glands we use practically the same procedure as Meland in giving preliminary heavy irradiation, using x-ray saturation or roentgen rays followed by radium packs, and then resorting to surgery if the glands do not retrogress and are surgically removable. This applies to single or isolated glands. If entire chains of glands are involved the case is practically a palliative one in almost every instance. In this connection it seems pertinent to call attention to the frequent use of surgical measures for the relief of pain.

One cannot leave this subject without dwelling upon the early recognition of mouth cancer. The elimination of important predisposing causes is also important. The dentist must help us out in both of these respects.

Dr. Lawrence Taussig, San Francisco, Calif. Neoplasms of the oral cavity are among the most frequent malignancies and on account of their accessibility they should present a relatively good prognosis. There are two reasons why this is not true. In the first place, most of them are of a very malignant type and in the second place, the lay as well as the professional public has not been sufficiently educated as yet to the necessity for early treatment. As is the case in malignancy elsewhere, the prime requisite for a good result is early as well as efficient treatment. I am quite certain that a very large percentage of malignant growths of the oral cavity are curable by several different forms of therapy, always providing that treatment is begun in the early stages of the disease. It is of course valuable to attempt to discover by comparison of statistics, which particular form of therapy gives the largest number of cures, but the fact will always remain that good surgery is preferable to indifferent radiotherapy and that efficient surface irradiation is superior to insufficient intratumoral irradiation. These papers, presented by men with extensive experience in this field, show the wide divergence of opinion and the lack of any definite standardization which still exists. The choice of the particular technique remains a matter of personal opinion and experience.

My own experience leads me to believe that each case must be considered individually. It is necessary to differentiate at the outset between those cases in which we feel that there is a chance to obtain a cure, and those in which palliation only is likely. In the latter group much harm may be done by excessive treatment in the way of increasing the suffering of the patient and even hastening the inevitable end. Palliation may be obtained by deep roentgen therapy, by surface or intratumoral radium applications, by electrothermic destruction or by partial operation, and the choice must depend on type and location of the growth and also on the physical condition and type of patient as well as on the experience of the physician. In the early and probably curable cases I do not believe that any hard and fast line of procedure should be laid out. In the majority of instances I prefer to irradiate the growth by the insertion of gold seeds of radon, followed in two weeks by electrothermic destruction of the area. This procedure apparently increases the number of permanent cures and materially decreases the time of suffering which the patient is forced to endure. Involved regional lymph nodes should be removed surgically when this is feasible, preferably after irradiation by radon seeds or deep roentgen therapy.

Dr. George M. Dorrance, Philadelphia (by invitation). There are one or two things I think the mouth surgeon misses. One is the general condition of the patient. I think if you will watch this more carefully it will save you a considerable number of cases. I have been associated with a number of these patients and in some instances get good results, while in others I do not. Whether syphilis is more common in Philadelphia than in New York I do not know, but our syphilitic patients do not respond well to treatment. I think these cases should be omitted and if you do that you will have a different class to publish.

My feeling is that after radium therapy has been used for a time, if the patient does not do well we should go back to the electrocoagulation therapy and remove as much of the growth as possible. We have heard of the very heavy dosage, of the treatment with gold seeds and without gold seeds; they all do well in certain types. It is the type, after all, that decides whether treatment will prove successful or not.

As to the glands of the neck, Dr. Pancoast and I went over those a number of years ago. We put in glass seeds for a time, and since then I have inserted quite a large number of gold seeds. I have watched my friends give a large amount of radium therapy, with varying results. I think we should stay away from the digastric if possible, and believe this will lower the mortality considerably. My mortality has been rather high in block dissection of the neck.

I appreciate very much the invitation to be present and discuss this symposium.

Dr. Quick (closing). I am very deeply grateful to the gentlemen who have presented their theses to us today and to those who have taken part in the discussion as well. After the very full manner in which the discussion has been covered it leaves but little to be said in conclusion.

I cannot help recalling a similar group of papers presented before this Society at one of its meetings about ten years ago. The contrast is striking, to say the least. It is evident that the viewpoints of various operators have come much more closely together and that there is today a grasp of the fundamentals of radiation recognized and accepted by all, that were scarcely thought of a few years ago. It is particularly interesting to note that whatever the individual equipment employed may be, there is nevertheless a striving for the adaptation of that equipment to production of a certain dosage intensity. It is generally recognized that dosage below a fairly well established minimum quantity at least, is of no value other than from a palliative standpoint. Far less stress is being placed upon the individual applicator of this, that or the other type except insofar as it has a bearing on the technical facility of application.

The problem in the minds of all today is that of getting from the equipment available a quantity of radiation which measures up to at least an adequate dose. In determination, in a broad, general way, of what we now regard as a minimum standard quantitative dose, we are very deeply indebted to our associates, the physicists and pathologists.

After all, ideal equipment is scarce if, in fact, it is available in its entirety at any special center. I refer particularly to radium equipment. Therefore, that which is available to the individual operator must be so adapted from a physical standpoint as to give the maximum of efficiency. This is recognized and being rapidly made effective. The small haphazard doses of a few years ago are being replaced by substantial doses under proper physical guidance and designed to influence tissue at a depth rather than to produce only visible surface reactions. No matter how we may differ in details, this fact is evident with all operators. We are coming to be more and more dependent upon the pathologist for aid in deciding the most advantageous general technical methods to be employed in the individual case. It is true that no histological slide rule has been developed to determine from the slide under the microscope just the exact dosage to be employed in every instance to give the ideal result.

In his effort to emphasize this, I fear that Dr. Stewart may have given the impression that little was to be gained as a guide to treatment through histological study of the tissue preliminary to treatment. I am sure that this was not his intention. I feel that he was simply attempting to sound a substantial note of warning against blind dependence on the microscope alone. He has emphasized a number of very important contributory facts which enter into the entire complex by means of which, as we now understand the situation, we determine the relative radiosensitivity or radioresistance of a given tumor. He has enumerated the most important local and general factors and has made very timely reference to the different anatomical locations, particularly the difference existing between the oral cavity proper and hypopharynx.

Pressing this point one step further brings us to the realization that to be of most assistance in the treatment of cancer today the pathologist must come more closely in contact with the clinical material—the actual patient—in order to render the greatest possible service. In other words, he must become at least something of a clinician.

It is perhaps true that the only safe dose of radiation to employ is the maximum dose. However, if the intensity of radiation for a given radiosensitive tumor is not necessarily great it at least affords us the opportunity of handling it by intensive external irradiation and foregoing some one of the implantation techniques entirely. The histological differentiation has also a tremendous bearing on the ultimate prognosis which may reasonably be anticipated and this in turn has its bearing on the vigor with which we might reasonably press subsequent treatment if dissemination occurs.

Dr. Widmann's presentation of the very

heavily filtered contact applicators is intensely interesting. Again it is another expression of an attempt at greater physical accuracy with a minimum of trauma to the tissues in the carrying out of this intensive irradiation. The prolonged character of his treatment is in keeping with what we have believed for years to be one of the chief factors of value in direct implantation of emanation. Is the explanation of his excellent results obtained by this method to be looked for on a purely physical basis? To me it suggests a very definite and distinct biological reaction. I doubt very much if we can explain the effect produced on purely a quantitative basis. The prolonged character of the irradiation and particularly the "broken dose" method of its application are undoubtedly very important factors. Contemplation of the various methods of breaking and prolonging dosage, no matter what the technical manner of application may be, is a very fascinating study and one which I believe we are only beginning to recognize in a very primitive fashion. Possibilities for the application of this principle with both contact and distance applications of radium as well as with roentgen radiation are very great indeed.

I believe that the paper by Drs. Martin and Sharp has answered a number of the points raised by Dr. Grier relative to the dangers of interstitial irradiation with filtered radon, and I might stress, in addition, the necessity for scrupulous care under all circumstances within the mouth no matter what the method of treatment may be, but particularly when radon implantation is a part of the program. The reaction of tumor tissue in the presence of infection is quite different and much less satisfactory than it is when the mouth is reasonably clean. Cleanliness can only be obtained by rigid, routine care in a department thoroughly organized for the purpose. I do not believe that time is lost in thoroughly cleaning up the mouth before any local treatment is applied. It can very well be done while the initial external irradiation is being carried out. I should like to mention also the possibility of protecting a great deal of the mucosa of the mouth from interstitial irradiation by specially constructed dentures. This work has been developed for some time now in our department by our dental resident and has been of tremendous value.

Relative to the treatment of the neck, I believe we all recognize it as perhaps more important in a relative way—certainly so in a great many of the cases—than the treatment of the primary growth itself. I believe it is safe to say that more cancer clinicians are coming to take a more conservative view of this problem of the treatment of the neck as time goes along.

From Dr. Simmons' paper and figures presented, it is evident that but a very small percentage, at best, of cases coming routinely under observation are amenable to the classic surgical procedure which has generally been accepted in the strictly surgical field for nearly a generation. With more accurate knowledge of dosage intensities, with the aid of histological differentiation as a guide to the probable intensity required and with improving external irradiation it would seem that less and less of radical neck surgery is indicated. If, however, neck surgery for removal of involved tissue is to be done, I should very strongly favor clean, sharp dissection rather than recourse to some of the newer cautery measures. It is true they have their appeal but I question very much if in proximity to so many vital structures the employment of such measures can be regarded as sound technical surgery.

Relative to the *external* irradiation of the neck I should like to sound a note of warning against too much dependence upon radium as a source of energy unless very substantial amounts are employed. It would seem to be much safer, particularly from the physical standpoint, to lean more heavily upon roentgen radiation. The possibilities attendant upon the vigorous use of external irradiation, largely roentgen radiation, and to a more limited degree radium —and this only because of its scarcity—is a fascinating problem and I feel confident that a few more years will show us a very startling advance in that direction.

What we refer to as a "dose" today is really a misnomer. What we actually mean, for the most part, is that quantity of radiation which the normal tissues of the tumor bed will tolerate without undue and permanent damage. We know very little indeed of the timing, the frequency, the intensity per exposure, the duration of individual exposures and total treatment interval incident to the best results to be obtained. Contemplation of the possibilities attendant upon a more accurate knowledge of these and other associated factors affords at least many interesting possibilitites for the future of this type of therapy.

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THE ROENTGEN TREATMENT OF CHRONIC LEUCEMIA*

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INTRODUCTION

IN the study of chronic leucemia two questions are likely to arise: (1) Why do some patients respond to radiotherapy so much better than others with the same general blood picture? (2) What is the best method of using radiotherapy? At the present time there is far more theory than fact to support any explanation of the first problem and as this paper is limited to therapeutic results, we will consider this only as it comes up in reference to special cases.

There is no gainsaying the striking temporary results obtained by large doses of roentgen rays over the spleen and lymph nodes in both types of chronic leucemia. There is, however, much to be said about the length of time that this apparent benefit lasts. It seems to us that small doses at frequent intervals produce excellent results, and we think the improvement, though gradual, is more enduring.

LITERATURE

Since the literature on this subject is much too extensive to be covered in detail here, we have selected only a few references which we consider of special interest.

Peabody, using radium, noted a decrease in abnormal forms of leucocytes. He also said that it was easier to produce an initial reduction in the total number than to keep the count low.

Oppenheimer, as well as Jenkinson, questioned the permanency of the improvement and was sure that harm could be done by large doses. Gulland agreed with this and said: "The more energetically a case is treated, the more certain it is to recur."

Minot and his coworkers give an excellent and detailed study of myelogenous leucemia in one paper[5]; in the other[6] the question of radiotherapy is discussed, more in regard to the effect on the blood cells in general than in leucemia. This latter contribution has an excellent résumé of the literature.

Epstein not only advocates small doses, but says that each patient is a separate problem. Dole also prefers the smaller doses.

MATERIAL

The following observations were made on 47 cases. Twenty-four were myeloid leucemia and 23 were lymphatic leucemia. We have not referred to any cases that were considered acute and have only reported cases that were adequately studied. No attempt has been made to record only satisfactory cases. All of these patients were in the Presbyterian Hospital or Vanderbilt Clinic within the last ten years, but this is by no means a complete list of leucemia patients treated in these institutions during that time. It is rather a series of patients whom we personally had an opportunity to observe and treat with roentgen rays.

TECHNIQUE OF RADIOTHERAPY

In lymphatic leucemia the cervical, axillary and inguinal areas are treated with medium voltage rays (approximately 125–135 kv., peak), 3 mm. aluminum filter and a 10 inch target-skin distance. Two-thirds to three-fourths of an erythema dose is applied over one area at one sitting. The most prominent nodes are selected for the first treatment. The patient returns once or twice a week, usually once. Only one

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area is treated at a visit. A blood count is made before each treatment. If the mediastinal or abdominal nodes are involved, high voltage rays (equivalent of 200 kv., peak) are used, with 0.5 mm. copper filter and a 50 cm. target-skin distance, one-eighth of an erythema dose being applied at one sitting.

any unpleasant reaction. Subsequent treatments are controlled entirely by the patient's condition and the response of the blood. If the cell count comes down very slowly, as much as one-fifth of an erythema dose may be applied at one sitting. The treatments are continued until the cell count comes down to fifteen or eighteen

List of Cases and Summaries
chronic lymphatic leucemia

Case No.	Hosp. No.	Age	Onset	Admission	Death	Illness	High Count	Low Count	No. Treatments
1	43679	68	8 mo.	10/20/19	6/18/20	16 mo.	146,000	23,750	21
2	55432	38	6 mo.	10/25/22	12/14/22	7 mo. 3 wk.	12,500	4,300	1
3	53736	66	1 mo.	3/18/22	6/27/22	4 mo.	56,000	9,000	7
4	61436	57	6 mo.	11/17/24	12/ 2/24	6 mo. 2 wk.	217,000	135,000	4
5	46946	38	1 yr.	8/ 4/20	12/17/22	3 yr. 4 mo.	700,000	385,000	48
6	51869	59	1 yr.	11/ 9/21	5/27/23	2 yr. 6 mo.	112,000	5,600	10
(IV) 7	138527	41	2 yr.	7/28/25	Living	6 yr. 10 mo. +	16,200	7,000	19
8	58812	56	7 mo.	12/27/23	3/22/24	10 mo.	27,000	7,000	6
(I) 9	68163	56	5 mo.	3/ 5/27	3/27/29	2 yr. 5 mo.	360,000	22,000	58
10	59854	60	5 mo.	5/ 6/24	12/27/25	2 yr.	8,000	8,000	5
11	323	66	—	4/ 9/24	Lost	4 yr. 4 mo. +	43,000	19,000	11
12	55346	59	1 yr.	1/13/22	12/ 8/22	1 yr. 11 mo.	6,300	1,300	5
13	49008	37	3 wk.	2/ 2/21	Lost	5 yr. 6 mo. +	200,000	8,100	41
14	68993	18	6 wk.	6/ 9/27	8/29/27	4 mo.	200,000	36,000	2
15	41034	63	2 wk.	2/24/19	2/11/22	2 yr.	257,000	4,100	13
16	53439	69	5 mo.	3/23/22	9/12/26	4 yr.	128,000	5,600	7
17	53728	53	2 wk.	4/17/22	5/20/22	6 wk.	108,000	88,000	2
18	78578	62	4 mo.	1/21/29	2/20/29	5 mo.	70,400	4,250	5
(III) 19	189284	44	7 mo.	12/ 5/28	Living	2 yr. 1 mo. +	138,000	11,500	17
(II) 20	71990	38	3 yr. 6 mo.	6/21/28	Living	5 yr. 6 mo. +	72,000	17,000	26
21	66688	50	3 wk.	8/31/26	6/ 1/29	2 yr. 9 mo.	56,500	13,500	43
22	238714	32	2 yr.	1/ 4/30	Living	2 yr. 6 mo. +	153,000	61,000	15
(V) 23	77039	62	4 yr.	11/ 1/28	Living	5 yr. 7 mo. +	55,000	3,900	30

Cases Treated with Radiotherapy to June 1, 1930.
23 Cases: 17 male, 6 female.
Ages: 18 to 68 years. Average, 52 years.
Onset: 2 weeks to 4 years. Average, 10 months.
16 dead—5 living—2 lost to "follow up."
16 patients followed to death. Illness 6 weeks to 4 years. Average, 1 year 6 months.
5 patients living. Illness 1 year, 6 months to 6 years, 10 months. Average, 4 years 6 months plus.
2 patients lost to "follow up." Illness 4 years 4 months to 5 years 6 months. Average, 4 years 11 months plus.
High Count: 700,000 to 5,500. Average, 136,600.
Low Count: 385,000 to 1,300. Average, 38,200.
Number of treatments: 58–1. Average, 17.

Myelogenous leucemia is treated with high voltage roentgen rays, as described above, applied over the spleen, usually with a 15×15 cm. field. One-eighth of an erythema dose is given at the first sitting, and the patient returns in a week for a blood count and the second treatment. This small quantity of rays rarely causes

thousand. They are then spread out over longer and longer intervals and are given just often enough to keep the blood count at the optimum point for the patient's sense of well-being. The importance of fairly frequent white cell counts is emphasized to the patient.

Owing to the difference in the suscepti-

bility of certain individuals the reduction in total number of leucocytes may be delayed, or the result of treatment may seem to be cumulative. Therefore at times white cells may be reduced more than is desirable This explains why we have some counts of 3000 white cells or even less.

of the disease as the leucocytes continued low and the patient died within six months. The cells increased a few thousand after a transfusion but never were over 5000; the final picture was one of cachexia and inanition.

Some of the lymphatic leucemias were

List of Cases and Summaries
chronic myeloid leucemia

Case No.	Hosp. No.	Age	Onset	Admission	Death	Illness	High Count	Low Count	No. Treatments
1	65630	57	1 yr.	4/23/26	9/15/28	2 yr. 5 mo.	870,000	29,000	50
2	44094	53	6 mo.	12/14/21	5/ 2/23	3 yr. 6 mo.	220,000	15,000	115
3	57770	26	2 mo.	8/20/23	8/27/27	4 yr.	168,000	1,000	16
4	67269	35	1 yr.	11/16/26	9/ 8/28	2 yr. 9 mo.	560,000	11,000	27
5	62737	45	1 yr.	4/27/25	Lost	3 yr. 3 mo. +	170,000	1,400	22
6	69159	48	2 mo.	6/25/27	5/ 1/29	2 yr.	282,000	25,800	27
7	47785	40	3 mo.	10/19/20	6/10/23	2 yr.	380,000	1,300	66
8	55633	21	3 wk.	11/20/22	3/15/25	2 yr. 4 mo.	493,000	17,000	68
9	49897	32	3 yr.	4/14/21	12/23/21	3 yr. 8 mo.	226,000	18,000	30
(IX) 10	61377	52	3 mo.	11/10/24	11/19/26	2 yr. 3 mo.	117,000	28,000	25
11	115133	32	8 mo.	6/19/23	2/11/24	2 yr.	340,000	18,000	16
12	41023	50	4 mo.	2/20/19	3/30/25	6 yr. 5 mo.	43,000	3,400	130
(VIII) 13	67088	56	2 yr.	11/25/24	11/ 1/26	4 yr.	360,000	11,000	31
(VI) 14	70729	34	1 mo.	2/10/25	2/26/28	3 yr. 1 mo.	120,000	19,000	60
15	64127	42	3 mo.	10/20/25	12/14/26	1 yr. 1 mo.	330,000	13,000	27
(VII) 16	63173	42	2 mo.	6/17/25	1/20/28	2 yr. 6 mo.	350,000	23,000	31
17	52590	34	1 wk.	1/13/22	7/ 5/27	5 yr. 6 mo.	34,000	4,800	11
18	81994	38	2 mo.	5/ 1/29	12/14/29	9 mo.	380,000	29,000	10
19	83839	48	2 mo.	6/19/28	Living	2 yr. 2 mo. +	300,000	17,000	25
20	63220	13	18 mo.	6/23/25	3/28/28	4 yr. 3 mo.	250,000	21,000	14
21	239125	37	2 yr.	12/28/29	Living	2 yr. 5 mo. +	300,000	94,000	6
22	244734	62	2 mo.	3/ 3/30	Living	5 mo. +	72,000	12,000	4
23	233657	49	4 yr.	2/19/30	Living	4 yr. 4 mo. +	318,000	48,000	6
(X) 24	233674	32	2 wk.	11/24/29	Living	6 mo. +	162,000	4,200	5

Cases Treated with Radiotherapy to June 1, 1930.
24 cases: 13 male, 11 female.
Age: 13 years to 62 years. Average, 41 years.
Onset: 1 week to four years. Average, 9 months.
18 dead, 5 living, 1 lost to "follow up."
18 patients followed to death. Illness 9 months to 6 years 5 months. Average, 3 years.
5 patients living. Illness 5 months to 4 years 4 months. Average, 2 years.
1 patient lost to "follow up." Illness 3 years 3 months plus.
High Count: 870,000 to 34,000. Average, 272,000.
Low Count: 94,000 to 1,300. Average, 19,000.
Number of treatments: 130 to 4. Average, 34.
Note: The number in parenthesis in front of the serial number indicates that the case is discussed in detail and the blood counts are shown graphically.

For example Case 3, Hospital No. 57770 has a low count of only 1000. This is, of course, far below what we would call a safe number, but this individual had the last treatment over a year before and at that time the white cells numbered 30,000. It is possible that this was a late manifestation

treated because of large nodes and white cell counts in two or three instances became lower than was advisable.

As the refractory stage approaches and the temperature rises, we give the treatments more frequently in a vain attempt to ward off the inevitable, but always use small

doses. In the face of a rising temperature, irradiation is useless but is usually continued on account of the psychological effect on the patient.

CASE REPORTS

To take up all of the cases in detail would make a contribution more detailed than interesting, so it has seemed wiser to discuss briefly 5 cases from each group, with a chart to illustrate the blood counts. Except for an occasional count, all of the blood work was done by one of us; two standardized pipettes were used for each examination; two drops were taken from each, and two counting chambers were employed. As a rule, 300 cells were counted for each differential.

CASE I. No. 68163. R. McC., an intelligent American business man, aged fifty-four, who had noticed a swelling in his neck for five months. He had lost 20 pounds. In addition to cervical lymph nodes the spleen was considerably enlarged.

White blood cells, 45,100; lymphocytes, 83 per cent.

He was treated with radiotherapy and for a time seemed to improve. The neck became smaller, he gained a little, but the white blood count continued to be high.

While under observation he was very much annoyed by "boils" and little areas of infection about the nose and lips. These lesions came

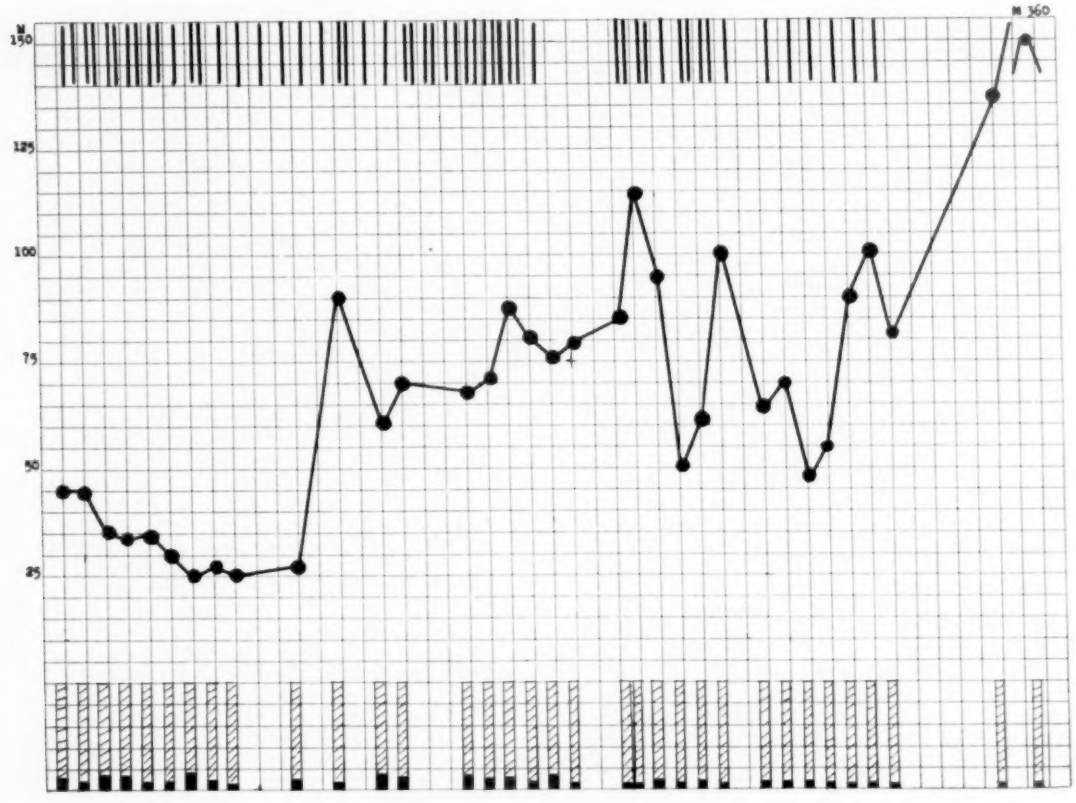

CHART 1. Case 1. The lines at the top of the chart indicate the radiotherapy, the line with large dots is the total white blood count, and the bars at the bottom of the chart illustrate the differential count, the hatched portion representing the abnormal cells, i.e., in the lymphatic cases the hatched portion represents the lymphocytes and lymphoblasts; in the myeloid cases the hatched portion indicates the myelocytes and myeloblasts. Each square is equal to 5000 cells when considered up and down; when considered from left to right they represent two weeks, so that any white cell count that goes over the top line is over 150,000 and every chart from left to right represents two years. We prefer to use one standard system even though several counts go well over 150,000 and some patients are followed for more than two years.

with no apparent cause and were difficult to treat. Sometimes similar spots would appear in the mouth and instead of healing, became covered by a soft jelly-like mass of what appeared to be fibrin. Transfusions were beneficial.

Although he cooperated in every way he became anemic, white cells continued to be too numerous, platelets became low. Two years after admission he developed a squamous cell epithelioma of the cheek, which resisted radium and roentgen rays.

A few days before death an extensive rash resembling chicken pox appeared, and there was also a purpuric eruption and swelling of the face.

The last treatment was given six months before death.

Comment. This is an example of a case of lymphatic leucemia for which little can be done. The low platelets (often about 20,000) contraindicated irradiation and transfusions were the only therapeutic agent.

Case II. No. 71990. M.K.G., a young American business man, aged thirty-eight, a graduate of the Naval Academy, came into the hospital because of sore throat, fever and general prostration. He had noticed swollen glands in the neck three and one-half years previously. His tonsils had been removed with only slight benefit. Four months before admission he was told he had leucemia and at another institution was given twenty-four roentgen treatments, frequently one every other day. The patient was sure he had been overtreated and rather thought his sore throat was due to this strenuous therapy.

When admitted the patient was obviously a sick man. The throat, roof of mouth and the pharynx were red and Vincent's organisms were present. The temperature was 103° F.; white blood cells were 17,700; lymphocytes, 97 per cent.

For about a week we were very apprehensive. The throat did not improve and several areas of necrosis appeared, the fever continued to run high and the patient was greatly prostrated. After two weeks, the fever ran lower and improvement was rapid and dramatic.

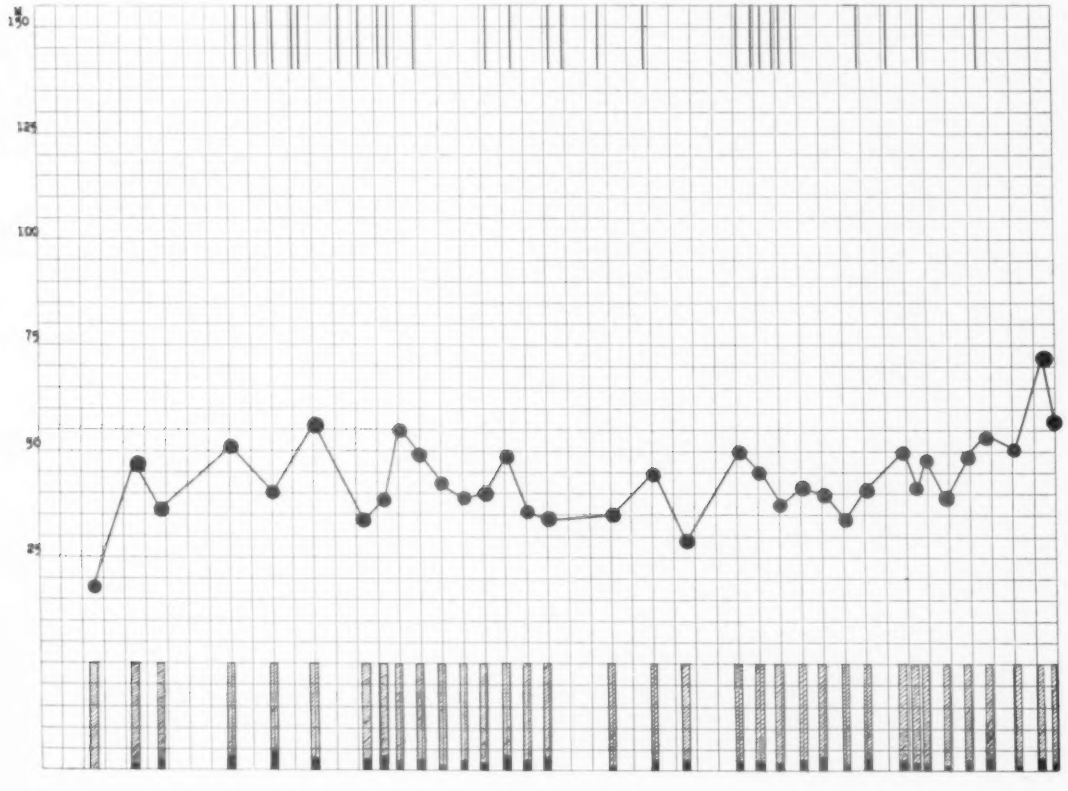

Chart II.* Case II.

* For explanation of chart, see Chart I.

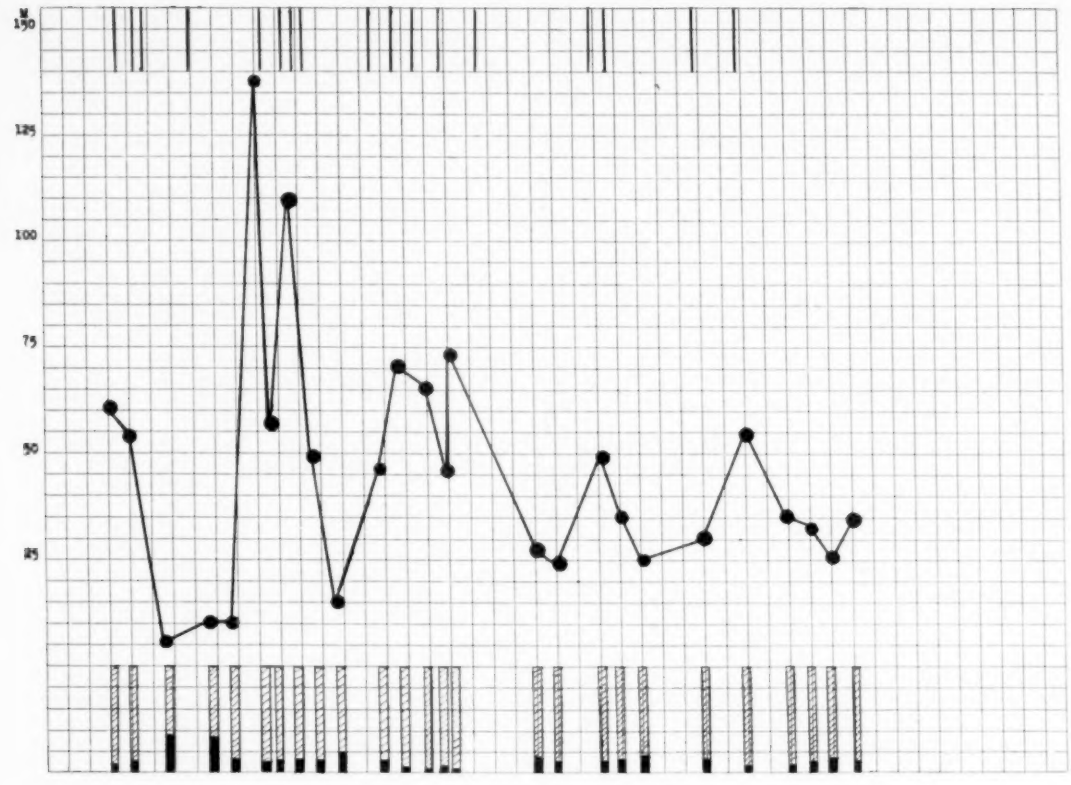

Chart III.* Case III.

Since then (about two years) this man has been active in business, carrying much responsibility and travelling widely.

He has been irradiated regularly. The white cells continue to be more numerous than normal (averaging in the neighborhood of 50,000). Platelets are usually below 100,000, but there has been no tendency to bleed, and he seems reasonably well and happy.

Comment. Considered in detail as a case of chronic lymphatic leucemia that recovered from a severe infection and after two years the patient is able to carry on.

Case III. No. 189284. I. H. G., an American architect, aged forty-four, who for six months had been "below par," "not sick," but as he said "only hitting on two instead of four cylinders." He was conscious of an enlarged spleen which at the time was easily felt 21 cm. below the costal margin. White blood cells were 60,000 with only 7 per cent granulocytes. The predominating cells were large lymphocytes and there were undoubtedly many monocytes. He was treated with radiotherapy and responded satisfactorily; in a month the leucocytes were within normal limits and he felt much better.

The spleen became smaller after the first few treatments, but has always been large. The patient is still reasonably active, he is not losing weight and the white cells have continued only slightly above normal with very little radiotherapy.

Superficial lymph nodes have never been conspicuous.

Case IV. No. 138527. M. K., a Polish tailor, aged forty-one, for two years had noticed that his neck was swollen. On his first visit he did not look acutely ill, but the neck was obviously enlarged. In the right posterior triangle there was one node that measured 4×2 cm. and several smaller ones. On the left side of the neck a similar condition existed, but the nodes were smaller. The inguinal nodes were somewhat larger than usual. The spleen was felt at the costal margin. The white cells were 27,000; lymphocytes, 86 per cent.

* For explanation of chart, see Chart I.

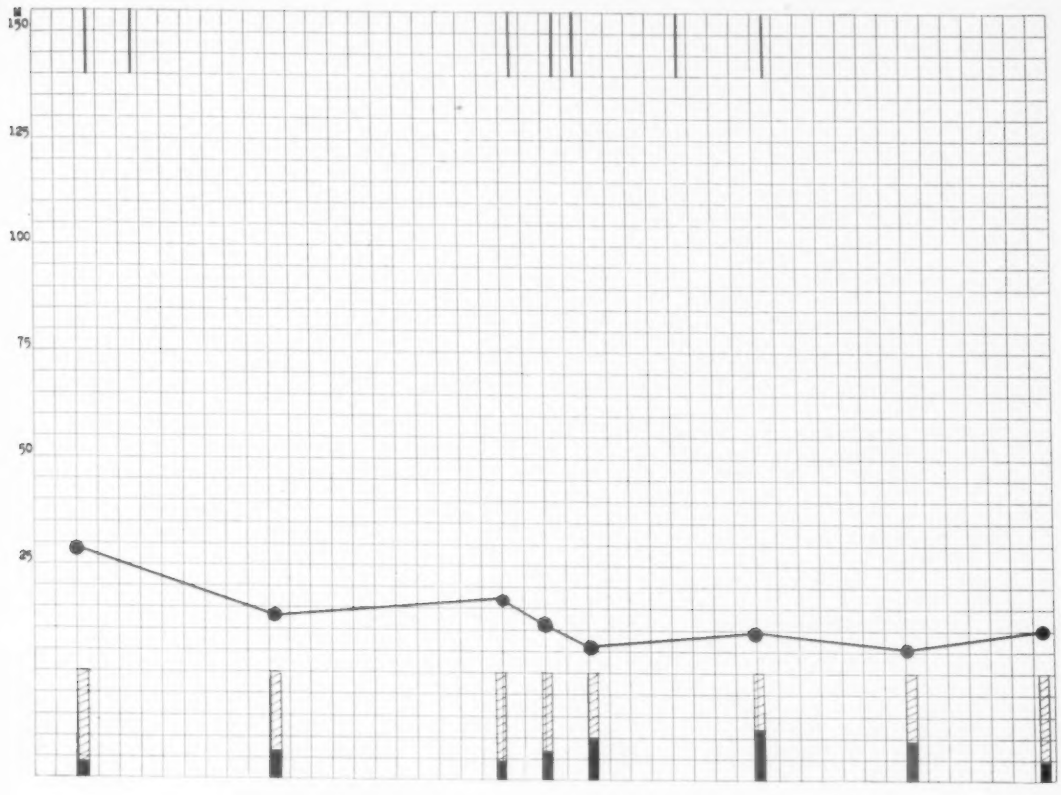

Chart IV*a*.* Case IV.

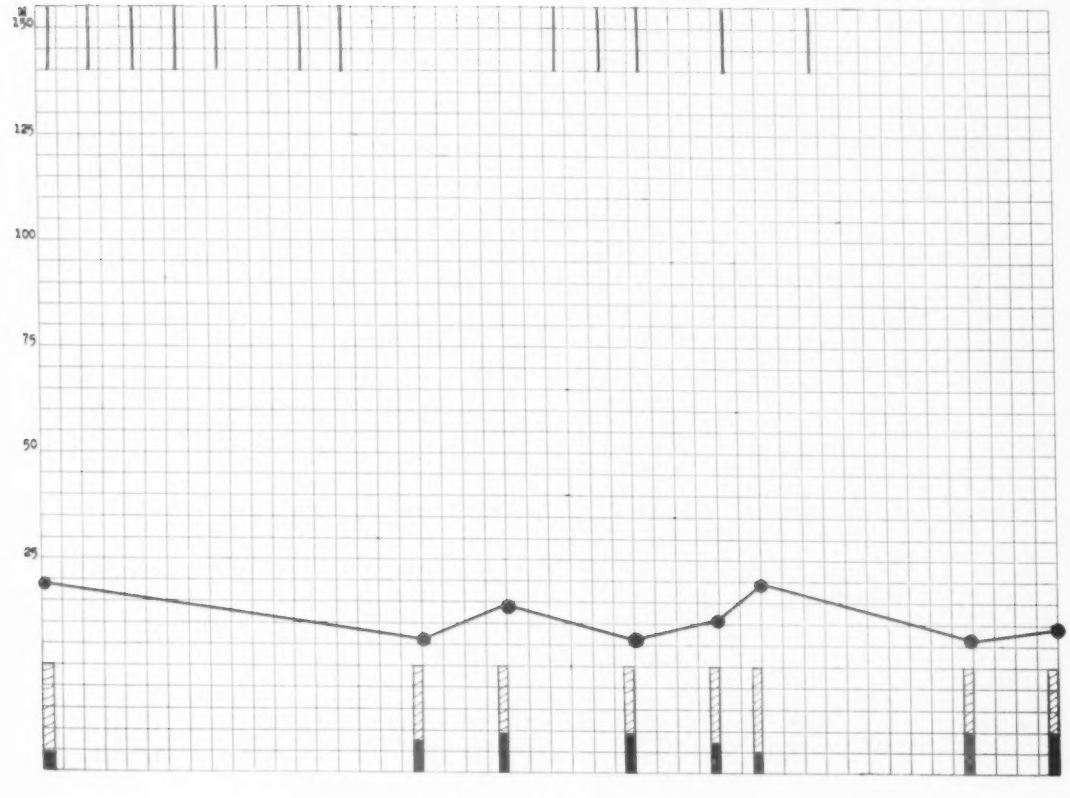

Chart IV*b*.* Case IV.

* In explanation of chart, see Chart I.

After five years the nodes show little change, the spleen is just palpable and the white blood count is 7,700; lymphocytes, 65 per cent.

Comment. This case is a good example of what we may be permitted to call a mild or slowly progressing form of chronic lymphatic leucemia. It is quite a contrast to Case I.

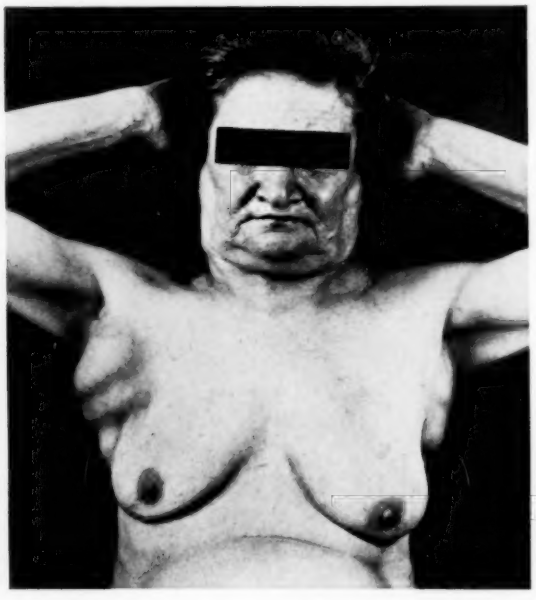

Fig. 1. Case v. On admission.

Case v. No. 77039. W. S., a Bohemian housewife aged sixty-two (with only moderate knowledge of English), came to the hospital because of large swellings in the neck and under the arms. Physical examination revealed a most unusual condition. On both sides of the neck were great masses of what seemed to be lymph nodes. A similar condition existed in both supraclavicular fossae. The neck just above the clavicles measured 47 cm. (18.8 in.). There were large masses in both axillae, the larger being on the right and measuring 9 cm. in diameter (Fig. 1). The inguinal nodes were also large. The edge of the spleen was felt 11 cm. and the liver about 8 cm. below the costal margin. Large movable nodular masses were easily felt through the abdominal wall and were probably abdominal lymph nodes.

In addition to the lymphadenopathy, the heart sounds were poor, the urine contained albumin and casts and the ankles were edematous. The white blood count was 38,000; lymphocytes, 68 per cent (mostly small).

The outlook was, to say the least, not encouraging. The first three or four treatments had little or no effect on the size of the nodes, but after the seventh and eighth exposures the masses seemed softer and began slowly to get smaller.

The patient feels better and is pleased with her improvement. Her weight has varied a little. She has recovered any early loss. The white blood cells are within normal limits; indeed we often wish they were more numerous to permit of more extensive irradiation.

Comment. We think this case is interesting, not that we can make any great claims as to permanent improvement, but after eighteen months the change is striking (Fig. 2). The neck is 9 cm. smaller and the axillary nodes are much smaller. She is not only up and about but is working regularly.

Fig. 2. Case v. After thirty roentgen treatments.

Case vi. No. 70729. A. N. S., a New York policeman, aged thirty, came to the clinic because of weakness and swellings in the inguinal region for one month. (As a matter of fact he had been advised to come by a doctor who thought his blood picture suspicious.)

On physical examination a few superficial

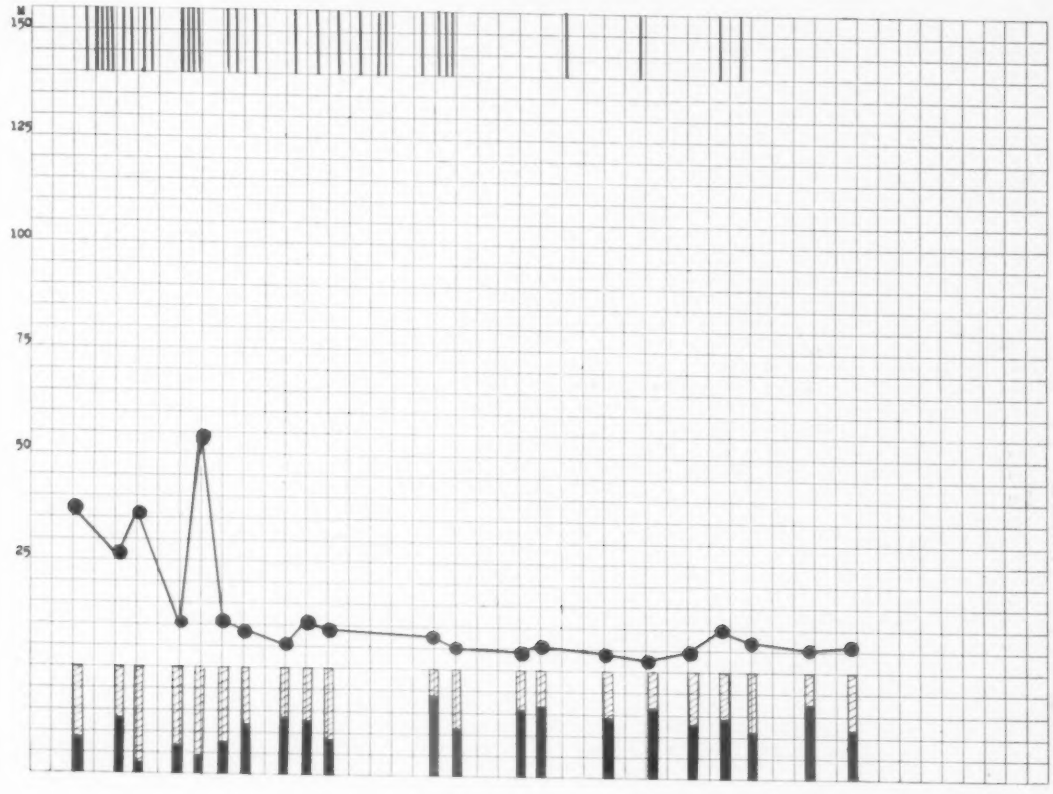

Chart v.* Case v.

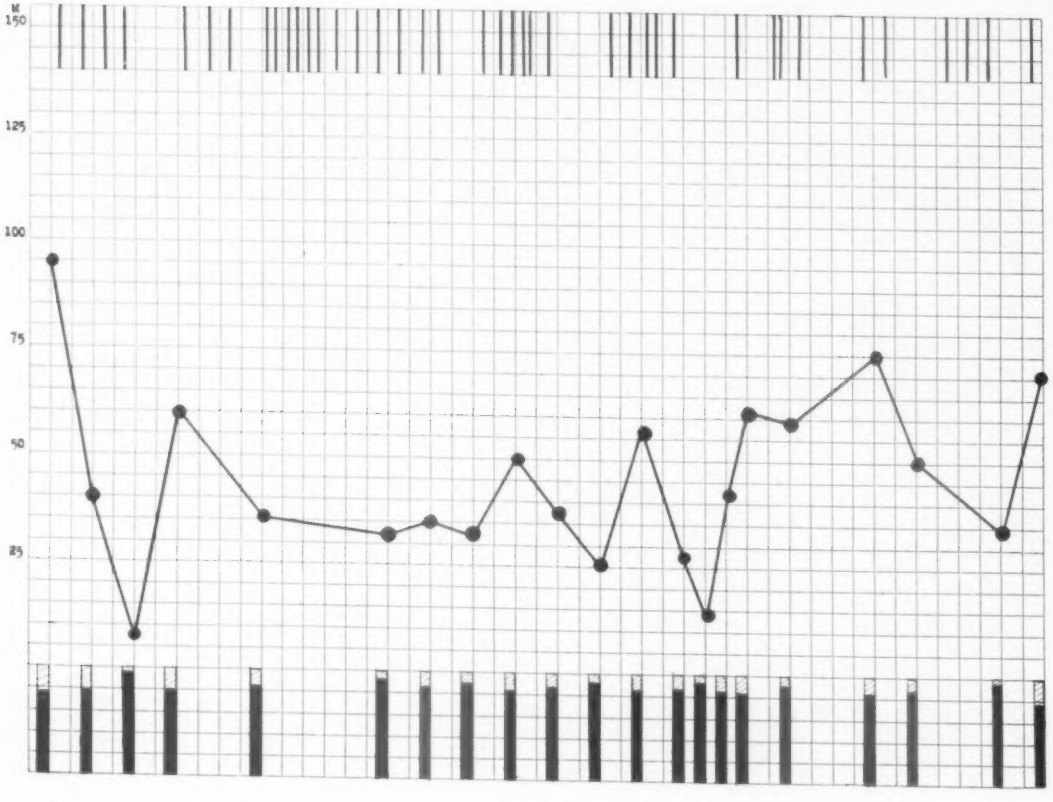

Chart via.* Case vi.

* For explanation of chart, see Chart 1.

lymph nodes were easily made out and masses about 3×1 cm. were felt in both inguinal regions. The spleen was felt 6 cm. below the costal margin. White blood cells, 95,000; neutrophiles, 62 per cent; eosinophiles, 1 per cent; young forms, 25 per cent, lymphocytes, 12 per cent.

He responded very well to radiotherapy and in two months the leucocytes were down to 11,000. He was treated regularly, usually every week or two, and in the meantime he was on active duty.

Three years after his visit he came in acutely ill, with fever, prostration, etc. Two weeks before admission his count was: white blood cells, 55,000; neutrophiles, 73 per cent; eosinophiles, 1 per cent; basophiles, 4 per cent; myelocytes and myeloblasts, 10 per cent; lymphocytes, 9 per cent; monocytes, 3 per cent.

He went down rapidly, the final illness lasting eight weeks. High fever, 102°–104°, and finally 107° F., with prostration, some bleeding of gums, and a shower of purpuric spots just before exitus. Three direct transfusions were of little benefit. A few days before death, the patient was given a small roentgen treatment and the white blood count dropped to 51,800. Whether or not this had any effect on the final result is questionable.

To sum up this case briefly: A policeman was first seen early in the course of his illness, he was irradiated frequently, evidently with benefit, he continued on active duty with only occasional slight interruptions, until within two months of his death.

There was one unusual feature which may be worthy of note. A section of one of the inguinal nodes was examined, but the pathologist (Dr. Stout) did not think it showed leucemia. Two months after the biopsy, the nodes broke down and on operation, pus was obtained, so it is at least possible that the swollen inguinal nodes had no direct connection with the leucemia.

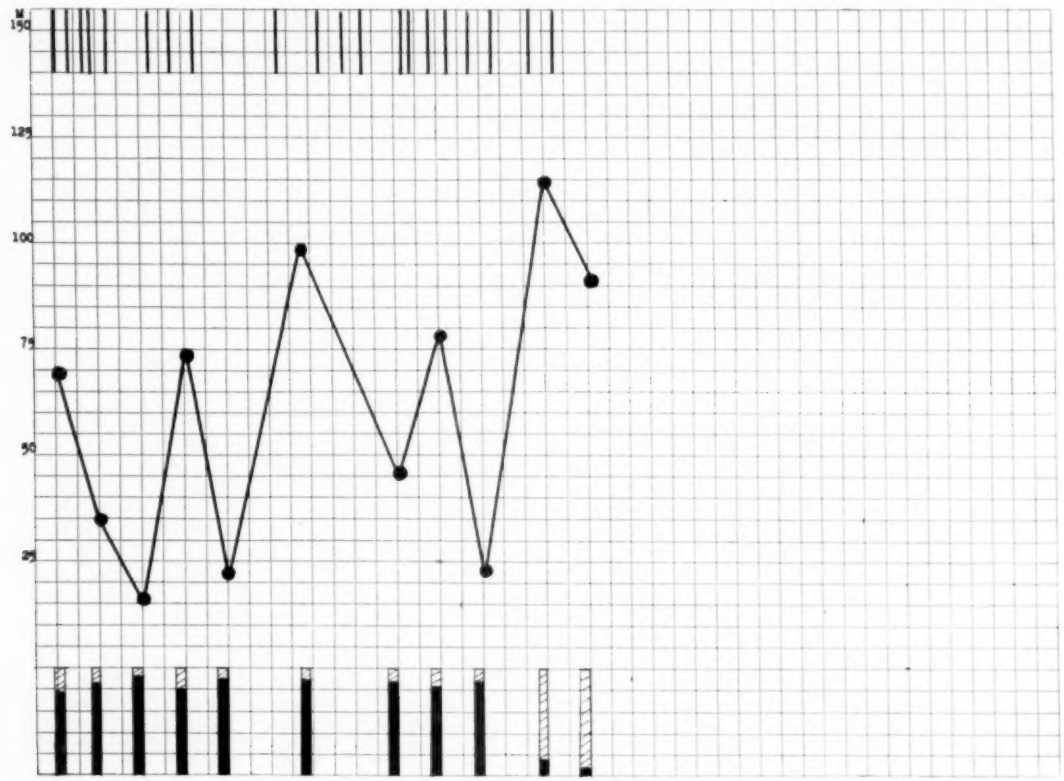

Chart vi*b*.* Case vi.

* For explanation of chart, see Chart 1.

Another point of interest was the sudden change in the type of leucocytes. Two months before death the granular cells dropped from 70–80 per cent to 10–15 per cent, the predominating cells were what appeared to be myeloblasts and were negative to oxydase stain. The final blood picture might have been confused with lymphatic leucemia.

lung and the sputum contained tubercle bacilli. The spleen was tremendous and filled almost all the left side of the abdomen. The blood count was as follows: white blood cells, 350,000; neutrophiles, 46 per cent; eosinophiles, 3 per cent; basophiles, 6 per cent; myelocytes, 25 per cent; myeloblasts, 14 per cent; lymphocytes, 6 per cent.

The patient lived out of town and it was difficult for him to make the trip; nevertheless, he

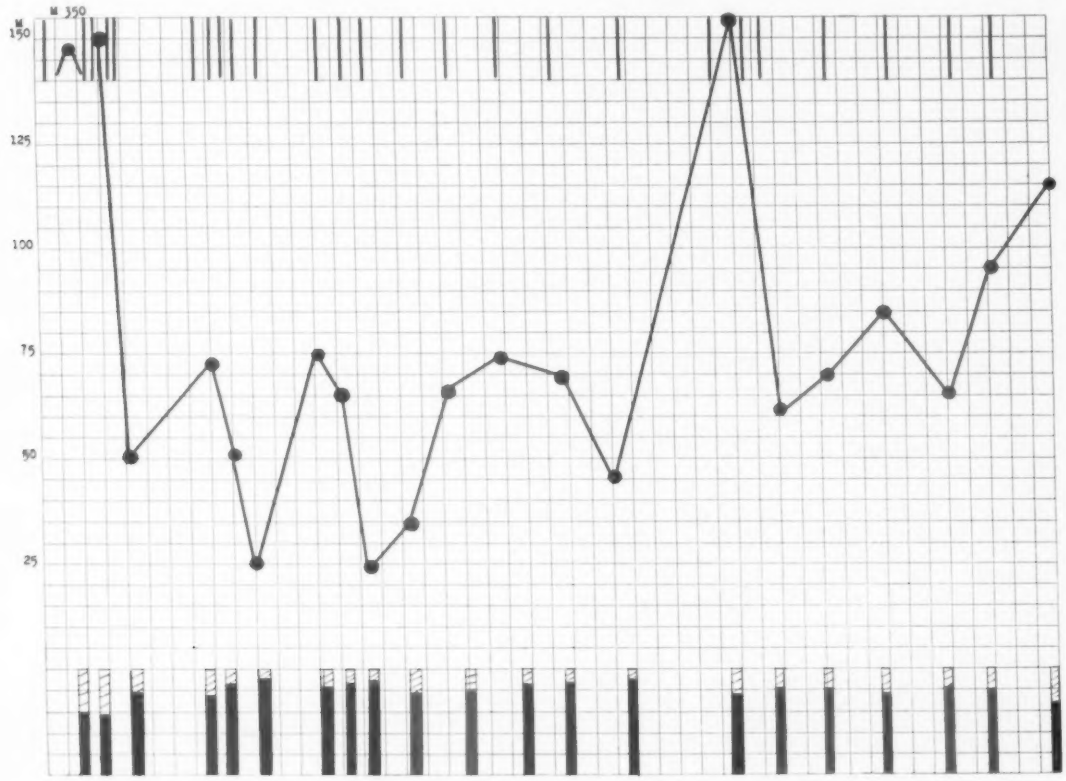

Chart viia.* Case vii.

Case vii. No. 63173. J. T., an American salesman, aged forty-two, came to the hospital complaining of a mass in the left side of the abdomen which was accompanied by pain radiating to the chest. There were also loss of weight, headache, and night sweats. His family history was significant: both parents, two sisters and one brother, all had died of pulmonary tuberculosis. Two other members of his immediate family were under treatment for this disease.

The man was thin and looked ill. There were signs of consolidation at the apex of the right

* For explanation of chart, see Chart i.

received his treatments fairly regularly. In five weeks his white cells were reduced to 35,000; young forms, 21 per cent. After eighteen months with only an occasional treatment, the white cell count had gone up to 150,000. He could not come for treatments as frequently as we desired and because of the pulmonary condition he wanted to be in the country. He died two and one-half years after admission. Our last white cell count was 220,000.

Comment. Here was a patient who, in addition to leucemia, had pulmonary tuberculosis. Although this is not an unusual

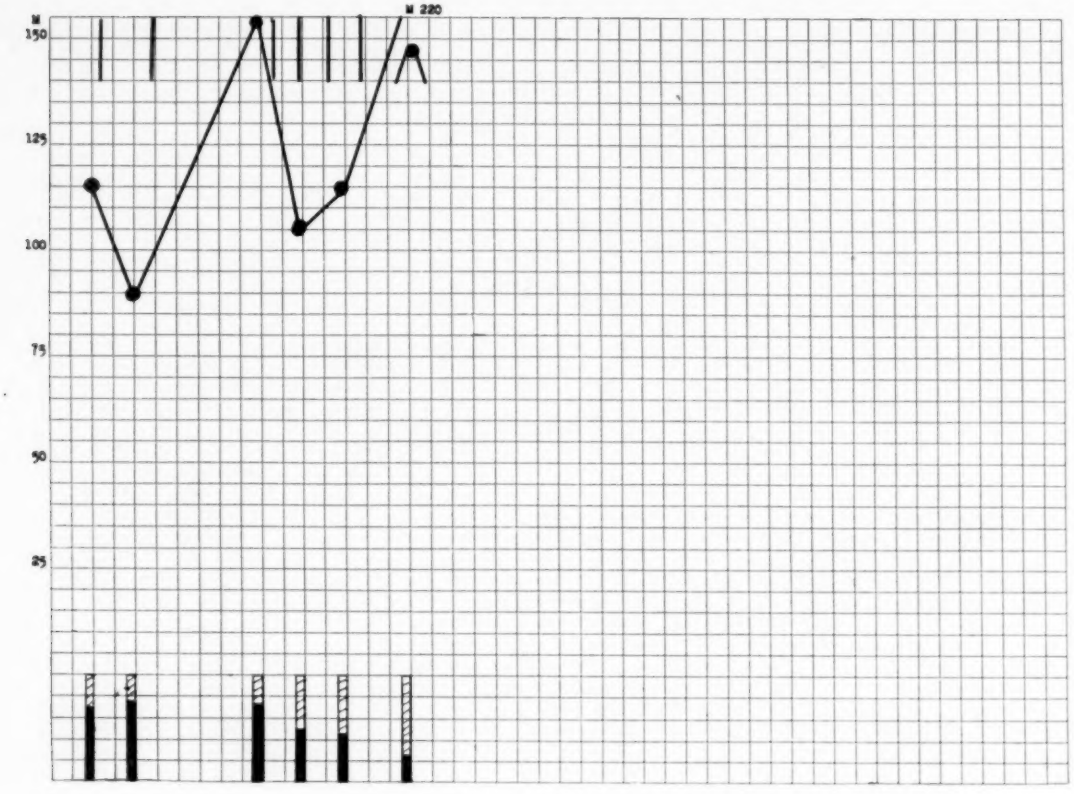

Chart VII*b*.* Case VII.

combination, it is one that makes therapy difficult. The problem was all the harder as the patient did not live in the city. With all these handicaps, this man was happy and active most of the time that he was under observation.

Case VIII. No. 67088. A. S., a negro, who said he was fifty-six, but looked older, came to the hospital with a two year history of a mass in left side of abdomen. He was troubled with gastric distress, weakness, and shortness of breath.

He had a large, hard spleen that reached to the umbilicus. The blood count was as follows: white blood cells, 360,000; neutrophiles, 58 per cent; eosinophiles, 5 per cent; basophiles, 8 per cent; myelocytes and myeloblasts, 20 per cent; lymphocytes, 6 per cent; monocytes, 1 per cent; unclassified, 2 per cent. He responded to treatment and did well for about one year. The white cells at one time were as low as 21,000, but young forms were always present.

For some reason he stayed away for six months and when he reappeared, the leucocytes were up to 280,000, with 27 per cent young forms. Although he received radiotherapy regularly, after this absence his white cells were never lower than 48,000.

On the occasion of his last visit he came into the hospital very weak, desperately sick, with a white cell count of 250,000. He failed rapidly, became comatose, and died one week after admission. Just before death the white blood cells were over 600,000.

Comment. We refer to this patient as he illustrates a severe and resistant type of leucemia. Although the disease was well established, he improved under treatment and it is just possible that had his treatments been more frequent, his life might have been prolonged.

Case IX. No. 61377. F. P., a Russian Jewess, aged fifty-two, had complained of weakness for three months. Examination showed a large liver and the spleen 10 cm. below the costal

* For explanation of chart, see Chart 1.

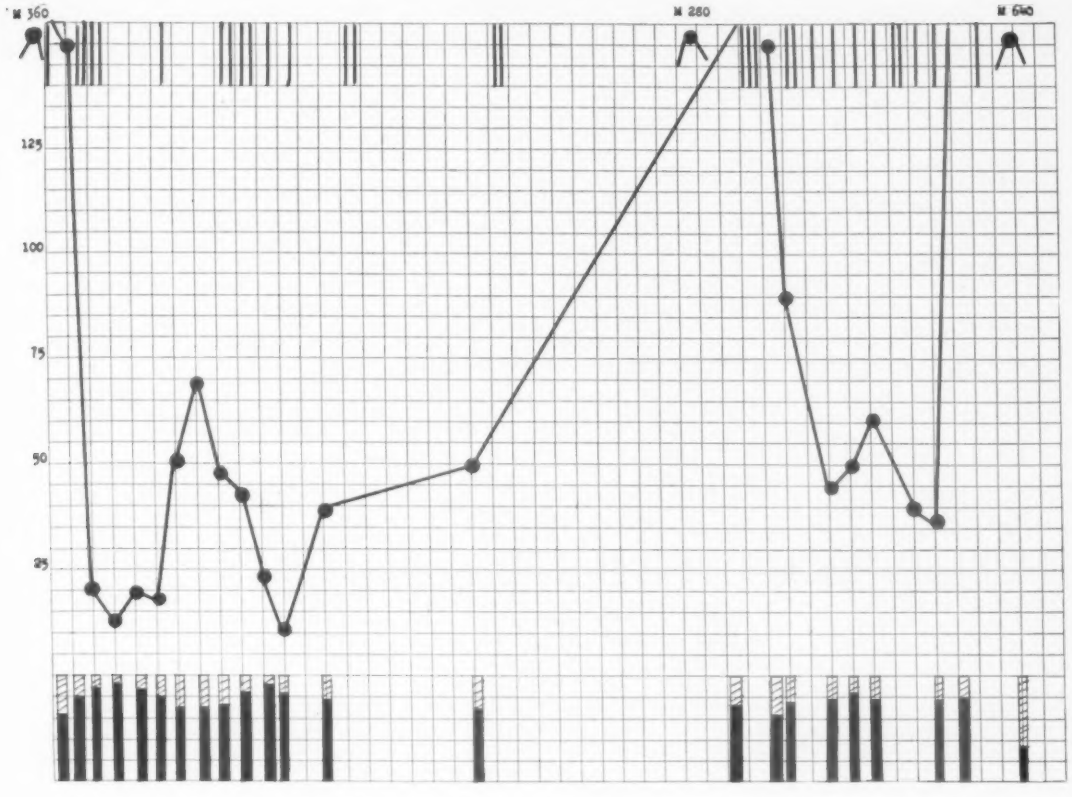

Chart VIII.* Case VIII.

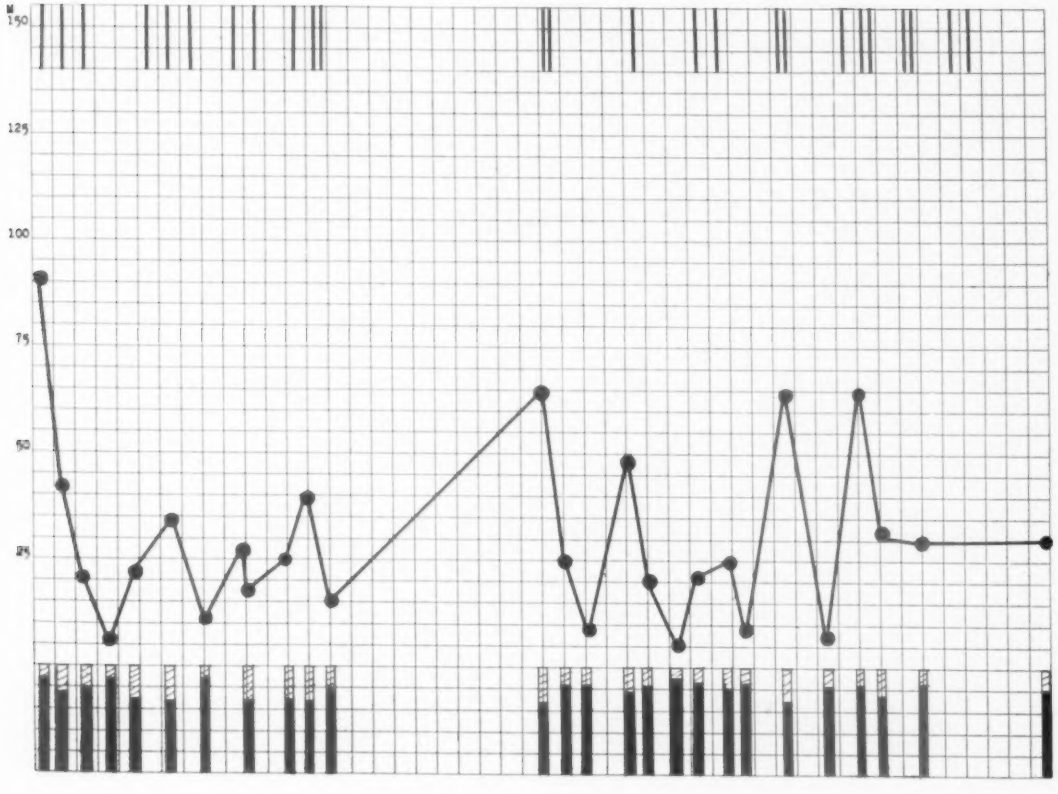

Chart IX.* Case IX.

* For explanation of chart, see Chart I.

margin. White blood cells, 90,000; neutrophiles 66 per cent; eosinophiles, 3 per cent; basophiles, 10 per cent; myelocytes, 11 per cent; lymphocytes, 10 per cent.

In six weeks she was given three treatments, with excellent results; the spleen became smaller and was felt only 3 cm. below the costal margin. The white blood cells were 8,500 with 12 per cent young forms.

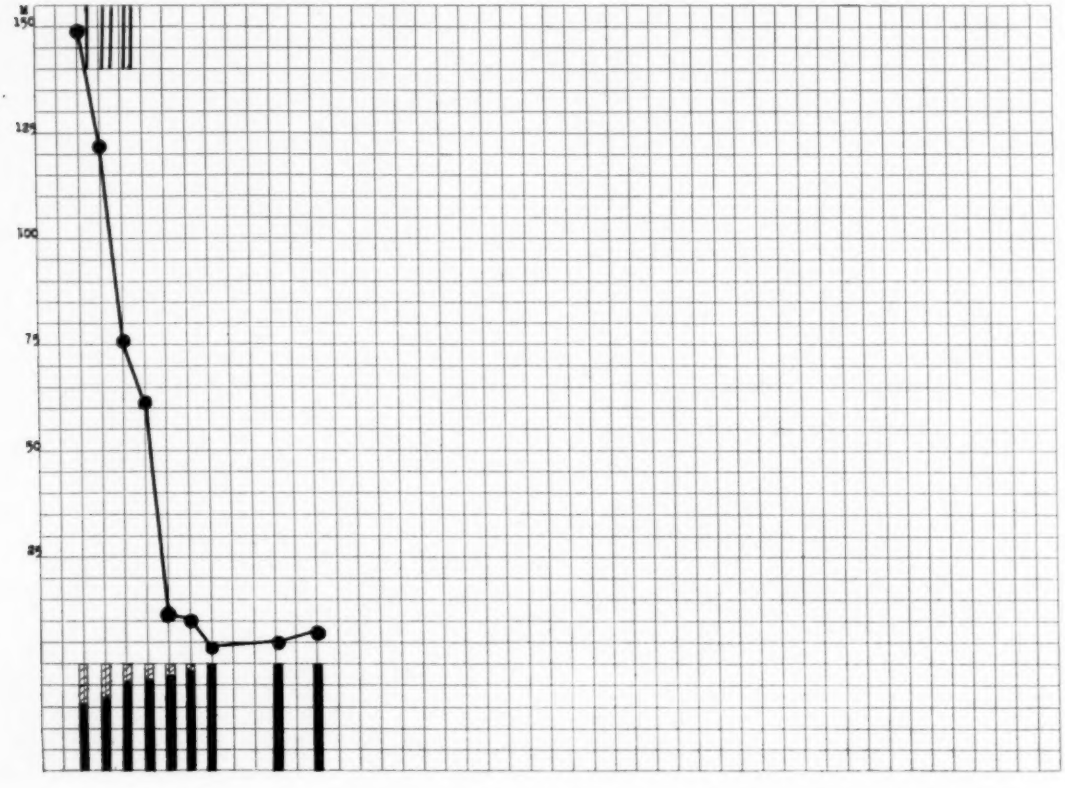

Chart x.* Case x.

After doing well for a little over a year she had an attack of "influenza," following which the spleen became larger and in three weeks extended 14 cm. below the costal margin; the white cells were then 65,000 with 30 per cent young forms.

This upset was probably the turning point in her condition. She was kept under observation, irradiated regularly, and given two transfusions, but the spleen remained large. The white cells varied but never ran very high; abnormal forms were always numerous. She died eight and one-half months after the attack called "influenza," which was severe enough to confine her to her home but about which we have no details.

Comment. We call attention to this patient for two reasons: The drop in the number of white cells was not accompanied by a decrease in the percentage of myelocytes, and it has been maintained by other observers that a slight infection will often prove serious to leucemic patients. Would this patient have continued to hold her own if she had not had some infection? We can only guess but the constant presence of abnormal cells is always a bad sign.

Case x. No. 233674. M. K., a young Jewish housewife, aged thirty-two, came to the hospital with a two weeks' history of a tender mass in the left side of the abdomen. She weighed only 98 pounds, 26 pounds below her best weight taken twelve years previously. She looked chronically ill. The spleen extended 5 cm. below the umbilicus, almost filling the left side of the abdomen.

* For explanation of chart, see Chart 1.

Hemoglobin (Sahli), 67 per cent; red blood cells, 4,000,000; white blood cells, 132,000; neutrophiles, 63 per cent; eosinophiles, 4 per cent; basophiles, 8 per cent; myelocytes and myeloblasts, 17 per cent; lymphocytes, 3 per cent; monocytes, 3 per cent; unclassified, 2 per cent.

Because of weakness and anemia she was given a direct transfusion of 500 c.c. of blood.

Radiotherapy was commenced ($\frac{1}{8}$ erythema dose over the spleen once each week). Within a month she had gained a pound. The spleen was smaller. The hemoglobin went up to 83 per cent; white cells dropped down to 62,500 with the differential count relatively unchanged.

In two months, although still weak, she was able to do her housework; the leucocytes were only 10,200 and there were 5 per cent myelocytes.

Within three months she had gained 9 pounds. The spleen was just palpable; white blood cells 4,200 and the myelocytes had disappeared.

After five months she had gained 12½ pounds, but had had an attack of "influenza" which caused a loss of 3½ pounds. At the end of six months, however, she had begun to gain again, she had no complaints and seemed to have weathered the little storm. The spleen was 3 cm. below the costal margin; white blood cells, 7,700; myelocytes, 1 per cent.

Comment. We have gone into a few details as this patient is an excellent example of what can be done with small doses of roentgen rays. It is not possible to prophesy how long this improvement will continue. We can at least look at the present picture with pleasure and hope for the future.

Only six roentgen treatments have been given. The last was given five months prior to the last blood count.

DISCUSSION

Statistics are often misleading and a glance at the lists of the patients is perhaps advisable.

An average of three years of life after the apparent onset of the disease in myeloid leucemia is probably no better than might be shown in any series of untreated cases; while an average of only eighteen months of life in lymphatic leucemia would seem to say little for the treatment employed.

We may be permitted to call attention to a few facts that change the picture materially.

Of the myeloid cases 5 are *still living* after an average of two and one-half years and one was "lost" to "follow-up" after three years.

There are a few other details that illustrate the fallacy of averages. Of the lymphatic cases, Case 2, hospital No. 55432, died suddenly at her home of what appears to have been edema of the glottis, certainly an unusual termination for a case of leucemia. This was nine days after the roentgen treatment over the spleen, the only treatment that she received. Case 10, hospital No. 59854, while apparently perfectly well, was killed in an automobile accident. Case 16, hospital No. 53439, died following an operation for carcinoma of the head of the pancreas. He was seventy-four years old.

The prognosis of some of these cases is far more difficult than would at first appear. To tell every patient that comes for treatment that he will probably not live more than a year or so is neither kind nor tactful. Granting the seriousness of the disease, we must also admit that some patients will do surprisingly well when radiotherapy is used intelligently. The size of the lymph nodes or spleen or both is often of as much significance as the white count itself. If the patient is in reasonably good condition, something can almost always be done, but if the heart or kidneys are seriously damaged little can be offered. Signs of fluid in the chest or abdomen are without exception danger signals that must not be ignored. A low platelet count with a tendency to purpura is usually a late manifestation and often indicates the approach of the end.

We hesitate to go into a detailed discussion of the blood cells but it is safe to say that the patients with the high percentage of abnormal forms are the worst risks. The higher white cell counts will sometimes respond remarkably to treatment, but the high white count with the low platelet count is cause for alarm. Different as these

two types of leucemia are, they have certain similarities when treated with roentgen irradiation. In the favorable cases there is not only a drop in the white cell count, but a reduction in the percentage of abnormal cells, which in the lymphatic form would be lymphocytes and lymphoblasts; in the myeloid form, the young granulocytes.

If the charts are consulted it will be noted that in Case I, although the white cells decreased under treatment there was very little variation in the proportion of cells, the abnormal always predominating—an unsatisfactory case. In Case II, the blood count showed little change; this might be called a milder form and occurred in a young man. Case III illustrates a satisfactory increase in normal elements. Clinically, however, he was doing no better than Case II. Case IV is a good example of the difficulty which may be encountered in trying to make hard and fast rules. This was a typical picture of leucemia but note the response to treatment, which was always given because of large lymph nodes, never for the high blood count. Case V illustrates in the blood picture the same improvement shown clinically (Figs. 1 and 2).

The blood changes in the myeloid type are often more impressive than in the lymphoid type, and we get a distinct impression that we can do more for these patients. Case VI with a moderately high count and about 25 per cent young leucocytes did well on radiotherapy, but abnormal forms never disappeared and just before death there was an overwhelming increase of myeloblasts. Case VII may be said to be a case that never really improved but nevertheless, was temporarily helped by irradiation. Note the steady increase in young forms as shown in the final counts. Case VIII shows to a striking degree the necessity of regular treatment. Not only did the leucocytes go very high, but the young forms also increased. Case IX is somewhat similar to Case VIII but the count did not run so high. Would not these patients have been benefited by more regular treatments? We think so, but cannot offer definite proof. Case X is interesting as it shows not only the drop in total white cells but the disappearance of abnormal forms. It is impossible to say how long this will so continue but we hope for the best.

Minot has said that it is not possible to increase the span of life by radiotherapy. As far as statistics go this is undoubtedly true, but we believe that the comfort and happiness which these patients experience is well worth the time and trouble required for treatment. Their life may be no longer but it is certainly happier.

Little can be learned by the initial drop in the white blood count. What is of tremendous interest is the change that appears after a time when radiotherapy loses its efficacy. Solution of this problem will go far to throw new light on this form of disease. Granting that we can only postpone the fatal termination, we should do all in our power to put it off as long as possible, and so conserve our only therapeutic agent that its value will be as enduring as possible.

CONCLUSIONS

Every patient is more or less an individual problem. A blood count should be made before each treatment.

Small doses of roentgen rays to the enlarged nodes and spleen in the lymphatic type, only one area at a time, and to the spleen in the myelogenous type are advisable.

The patient should be treated regularly, at first every week; later the period may be lengthened when the response and susceptibility of the patient have been established. Many do well with counts considerably higher than normal, but sometimes the cells will continue to decrease long after irradiation.

An occasional platelet count is advisable, especially in the lymphatic type. Purpura always contraindicates irradiation.

Although the prognosis is always bad, it is often well to await the result of a few

treatments before being definite as to prognosis.

In the myeloid type it has been said that 10 per cent or more young cells indicates a hopeless outlook; this may be true but if this percentage is reduced by radiotherapy the prognosis may be said to improve. The reduction in the percentage of abnormal cells is fully as important as the initial drop in the total count.

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DISCUSSION

Dr. Charles L. Martin, Dallas, Texas. When I was asked to discuss this paper it suddenly occurred to me that I had learned practically nothing new about leucemia during the past ten years. I then delved into the recent literature but did not encounter any large amount of new material. More investigation along this line is therefore very badly needed.

In listening to this very excellent paper the portion dealing with prognosis struck me as most interesting. I hope that Dr. McAlpin will tell us a little more about platelet counts in his closing remarks. He stated that a low platelet count is a bad prognostic sign. Perhaps he can tell us whether a patient may have a high platelet count in the beginning of the disease which becomes progressively lower as he reaches the point where treatment is no longer effective. As I understand him, most patients are likely to have either a high or a low platelet count from the beginning.

His observation that cases showing a drop in the percentage of abnormal blood cells during treatment do best is in accord with my own experience.

When I was a resident at the Massachusetts General Hospital, Dr. Denis, the chemist, and I studied the blood of leucemia patients receiving radiation therapy but we learned surprisingly little. We observed that the symptoms such as fever, headache, malaise and discomfort from an enlarged spleen were hardly noticeable so long as the white count remained below 100,000. As a result it has always seemed to me that the best plan of treatment consists of the administration of efficient doses as far apart as they can be given to keep the count below 100,000.

No doubt this can be accomplished by Dr. Golden's technique but it is certainly more convenient to give the treatment within five or six days' time and then to allow the patient to go his way until more treatment is needed. Even in lymphatic leucemia the involved glands can all be covered in eight to ten days.

I notice that nothing is said in the paper about the treatment of the long bones. My technique has always been that recommended by Pfahler and others, namely, the irradiation of the spleen through multiple ports of entry in myeloid leucemia. If Dr. McAlpin thinks therapy of the long bones is worth while perhaps he will be kind enough to explain his reasons to us later on.

The behavior of the red blood cells has in my experience been one of the best prognostic signs. A rapid disappearance of the secondary anemia after irradiation insures at least temporary improvement. For this reason our cases all receive a liver diet and a dram of iron and ammonium citrate given in a glass of milk after each meal until the red blood count approaches normal. It is my impression that this therapy is very valuable although I can produce no absolute proof.

I sincerely hope that the authors will continue their studies since they apparently have at their command an ample material.

Dr. H. K. Pancoast, Philadelphia. Most conditions treated by radiation during the past decade or two have shown improvements as a result of improved technique. It is unfortunate that leucemia is a condition which has shown practically none. The first case of leucemia was treated in 1902. I think the first report of a case treated was in 1903. I read the first paper on treatment of leucemia before this Society in 1906 and again in 1907. But in looking back over those years, I can see very little difference in the prognosis except as we have been wise in the selection of our cases, in the use of comparatively low dosage which has been stressed today, and in the elimination of the acute leucemia from our treatment list.

A few years after we began treating leucemias, we advocated the bone marrow treatment as primary to the treatment of the spleen. We have continued ever since 1906 to follow that procedure, because we have seen no better results obtained by any other method. I think all the methods that are used today give about equally good results, and we all are aiming to keep our patients in the best physical condition with as little treatment as possible, but with due regard to the economic problem. Applications to the bone marrow is not an economical method as compared to the treatment of the spleen, and in some instances in which it has not been possible to carry out treatment over the bone marrow systematically, we have exposed the spleen alone. These are very few in number, however.

I would like to hear a little more about the importance of the platelet count. I do feel that the red cell count is of extreme importance and when a patient shows a beginning and a persistent drop in the red cell count, that patient is not doing well and is going to go bad before long and one must let up in the treatment as much as possible and use measures toward the preservation of the red cells. Some of these have been mentioned already by Dr. Martin, especially the use of liver and iron, and, as we have often used in the past, small doses of arsenic. But beware of giving very heavy irradiation in the falling red cell count.

We usually attempt to get our earlier cases down to as nearly a normal white count as possible, with as nearly a normal differential count as seems safe, then we watch the patient carefully by a count at least once a month until there is very definite change, indicating a recurrence. Then we begin treatment again and keep it up until the patient returns to as nearly normal figures as is possible or seems safe.

These are all various methods of getting at the same end. It is very unfortunate that we in using an agent which seems to have such a very definite effect upon leucemic patients have been unable through all these years to improve our technique, or at least find one which gives very much better results than those which were obtained twenty-five years ago.

Dr. G. E. Pfahler, Philadelphia. I appreciate this paper and I appreciate all the difficulties that the speakers have already emphasized.

Up to twenty years ago, I too tried to treat both the spleen and the bones, but because of the increased expense of treating the bones without accomplishing any increase in results, since that date I have been limiting the treatment to the application over the spleen.

I wish to refer to a case that came under my attention about a year and a half ago which did not respond to high voltage roentgen rays applied over the spleen; in fact, the patient grew progressively worse during two weeks of treatment in which the applications were made in about 25 per cent doses nearly every day. Then we made an application with 200 mg. of radium in the form of a radium pack for forty-eight hours and immediately the white cell count came down and the patient started to improve and when the white cells dropped to 11,000, we then sent her home. She has made two trips since that. I saw her last week. She had returned approximately ten days previously because we have been having blood counts every two weeks, and when the white cell count reached approximately 22,000, she was sent back for treatment. We again applied the radium packs, but this time with the hope of making a success of what seemed to be a mere matter of recurrence. We have treated the entire time with high voltage roentgen rays, 25 per cent over the entire body except the head.

The patient went home and a few days ago was symptom-free and very happy. I am simply speaking of the fact that we were using high voltage roentgen rays in this case and got no response, but when we used gamma rays, 200 mg. of radium filtered through 1 mm. of platinum and 1 mm. of gold, at 4 cm. distance, over

the spleen, we got a very prompt response.

I do feel that we are probably all giving up too easily and that if we just strive a little harder, we will probably find some constitutional treatment that can be added to the treatment and make these cases a real success, at least that is my hope.

Dr. Ernest Kraft, Chicago. About a month ago, we had a child, eleven years old, with chronic myelogenous leucemia. There was a cell count of 660,000 leucocytes. The spleen filled most of the left abdomen. We gave her one deep roentgen treatment and the white cell count was reduced to 209,000 within twelve days. Then the child was discharged without our sanction. She made a long automobile trip and the mother reported to me that two days later the child had much pain in her legs and fever and was real sick. She was taken to Indianapolis for further treatment.

I mention this case since it is not known to me that chronic myelogenous leucemia will occur at such an age. May I ask the authors about their experience in this respect.

Dr. McAlpin (closing). In the first place, about irradiating the long bones, I don't know much about it. It just happens we haven't done it except in desperate cases. As a rule, we have irradiated the spleen altogether.

I think that a severe chronic myeloid leucemia in a young child is extremely rare. We had no young children in this series at all.

About the prognosis of leucemia, Dr. Martin very courteously asked something of a poser. I rather discreetly sidestepped that in our paper. There are certain points which will help you, but you frequently are upset by the ultimate outcome.

The reason I didn't discuss the red blood cells with more detail was that I became interested in talking about the white cells and it made altogether too complicated a chart to run the red cells and hemoglobin against the white cells. So we decided in this paper to consider white cells alone. Changes in the red cells often act as a warning, without question

Dr. Martin's treatment is perfectly sound and very well advised. We have gone so far as not infrequently to give transfusions and sometimes it seemed to help.

Prognosis in general is the prognosis of a chronic condition and not only a hematological disease. The patient with fluid in theh abdomen, fluid in the chest, and signs of decompensation, is obviously a bad risk and the blood count must not be considered alone. The large spleen as a rule, is a bad sign, especially in the myeloid type. We have all seen cases that have done well and the spleen has decreased in size. We have also all seen cases where the spleen hasn't gone down. The spleen that doesn't decrease in size is obviously a serious case, that is, from the standpoint of physical examination. The blood count that does not respond to radiotherapy has a bad outlook. That is what I meant when I said that if there is more than 10 per cent of abnormal cells present, the outlook is not *always* bad; wait until you see how the patient reacts to radiotherapy. That is important.

The question of platelets won't bother you much with a myeloid leucemia. I think that is a fair statement. If you do encounter a myeloid leucemia that in the beginning has low platelets, you can look out for trouble. They are very much more of a nuisance in the lymphatic. The case that tends to have purpuric spots and tends to bleed from the gums is always a bad risk and you can't do a great deal except perhaps give transfusions. I think that the weight, the general conduct of the patient, as has been indicated, is important. The patient who holds his weight, who lives a happy life and is contented and getting along pretty well is, of course, a good risk, as such patients are in any other disease.

Always remember, and I think this is important, if you give patients large doses and then slap them on the back and tell them to come back in six weeks or two months, they don't always know when their symptoms are getting worse. That is one thing of which I am perfectly sure. I have sent a patient home with the differential count absolutely normal, the hemoglobin was well up and the spleen was not palpable, and then in two or perhaps three months, when the patient and physician had both taken a vacation, the patient came back with a spleen 6, 7, or even 10 centimeters below the line of the ribs and the outlook very grave; right on top of that comes the picture of anemia. There is just one thing about the anemia. Sometimes you get this prolonged action; whether the irradiation has anything to do with it, I don't know. I doubt if there is cause for worry if the patient isn't bleeding. If the platelets have held up reasonably well, a transfusion or two will give just as dramatic a result as though the red cells had never gone down.

EXTREME DILATATION OF THE LEFT AURICLE*

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IN 1901 Sir Isambard Owen and W. J. Fenton reported for the first time a case of extreme dilatation of the left auricle. Since then 14 other proved cases have been reported (including the one reported below). Because the lesion can be accurately diagnosed roentgenologically, it seems worth while to call the findings to the attention of roentgenologists and clinicians, reporting a new proved case, tracing its development and reviewing the literature.

CASE REPORT

M. R., female, white, aged thirty-one, admitted for the first time on August 22, 1926, giving a history of a typical attack of rheumatic fever at the age of fifteen, with a recurrence about four months later. She apparently made an uneventful recovery. Four years later, however, she developed rather suddenly palpitation, precordial pain and dyspnea. She subsequently had repeated rheumatic attacks associated with palpitation and dyspnea, but was never confined to bed for more than six to eight weeks. Four years ago, i.e., twelve years after her first attack of rheumatic fever, she became edematous and was confined to bed for three months. Since this time she has been increasingly short of breath and her hospital admissions have been increasing in duration. On her last admission she was in extremus.

Physical Examination (Dr. R. W. Scott). August 24, 1926. The patient is a small woman weighing about 90 pounds. There is considerable edema over the sacrum and legs, although respiratory distress is not particularly marked.

Heart. The heart is a huge organ for the size of the patient. It extends to the posterior axillary line. The patient has been under digitalis for the past several weeks and now has what appears to be from palpation typical coupling. In the normal pulse following the premature beat is felt a characteristic diastolic thrill. There is marked activity also of the right ventricle. The left border of cardiac dullness is in the posterior axillary line, and there is dullness three fingers to the right of the sternum in the third and fourth intercostal space.

Over the apex the first sound is obliterated by a blowing systolic murmur, and in early diastole there is a loud diastolic murmur which ends abruptly and does not run throughout the diastolic cycle. This is the murmur that is felt as the very marked thrill. There is a very marked accentuation of the pulmonic second and a rather marked systolic murmur over the aortic area, where a definite thrill is palpable. There is a slight dullness at the right base, probably fluid, and in spite of the fact that there is considerable retention of body fluids, the lung fields are free of moisture. Definite ascites is present, but not enough to warrant tapping at this time. The pulse is definitely diminished in volume. No sclerosis of the arterial walls is demonstrable. No icterus of the sclerae. No definite anemia visible. No cyanosis of the fingers, although the lips are a little blue. The liver does not pulsate. The veins of the neck are only slightly engorged.

November 10, 1926. Over the base, particu-

FIG. 1. Extreme dilatation of the left auricle.

* From the Roentgenological and Pathological Departments of the Cleveland City Hospital, and University Hospitals, Cleveland, O.

larly to the right of the sternum, one feels a systolic thrill and on auscultation one hears a systolic murmur and a much fainter diastolic blow, which we believe originates at the aortic orifice.

The urine has varied in specific gravity from 1015 to 1033. There is often considerable albumin present, occasional casts and frequent white, and occasionally red blood cells, present. The red blood count varied from 4,960,000 on the first admission to 5,312,000 on the last. The blood pressure has varied from 108 to 130 systolic and from 65 to 72 diastolic. The blood Wassermann has been repeatedly negative.

Summary. Mitral stenosis with the aortic orifice somewhat involved, with probably definite narrowing. Marked hypertrophy of both ventricles. Auricular fibrillation.

Roentgen Report. August 26, 1926 (Fig. 1). There is a tremendous increase in the transverse diameter of the heart shadow. This increase is both to the right and to the left, but mainly to the right. On rotating the patient into the first oblique position under the roentgenoscope, a rounded shadow with fairly sharply defined borders appears in the right lung field from the posterior portion of the mid-chest. This shadow cannot be separated from the heart shadow. It shows only very slight pulsations. The retrocardiac space is obliterated. This shadow could represent the enlarged dilated left auricle. There is no change in the cardiac silhouette with a change in the position of the patient. Findings are those of an enlarged dilated heart, probably secondary to mitral disease with predominating stenosis; cardiac decompensation and a small amount of fluid at the right base.

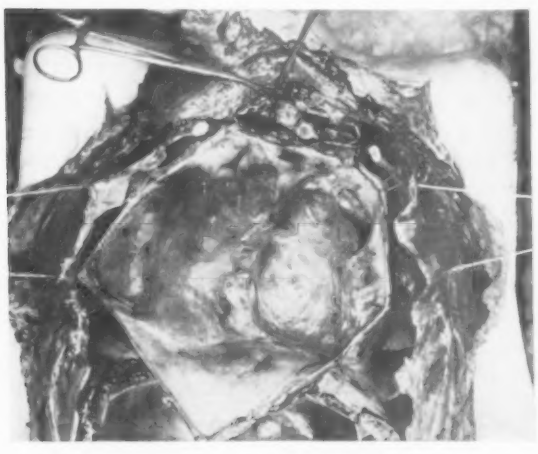

Fig. 2. View of the heart after reflecting the pericardium.

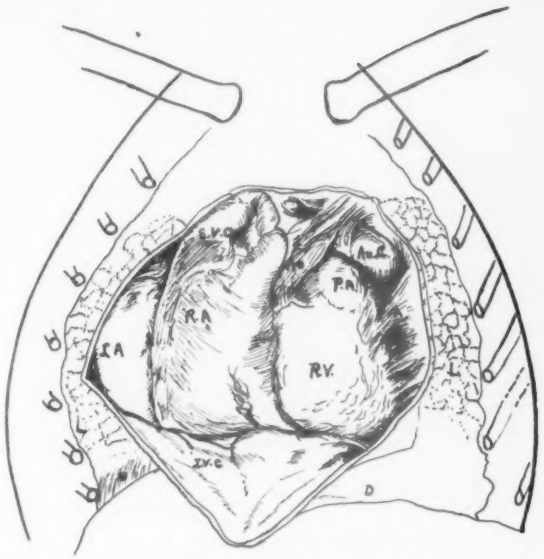

Fig. 3. Diagram of the findings at autopsy. LA—Left auricle. RA—Right auricle. RV—Right ventricle. AuL—Left auricular appendage. AO—Aorta. A—Adhesions. PA—Pulmonary artery. SVC—Superior vena cava. IVC—Inferior vena cava. D—Diaphragm.

Autopsy Findings. March 3, 1927. On opening the thorax the heart is seen to be enormously increased in size (Figs. 2 and 3). The pericardium is adherent to the sternum and to the left parietal pleura. Palpation of the heart before removal shows that the auricles are markedly distended, and one unusual feature, which is clearly demonstrated, is that the left auricle projects posteriorly and to the right, so that it actually forms the right border of the heart—projecting at least an inch beyond the right border of the right auricle. The widest transverse diameter measures 21 cm. The leaflets of the pericardium are densely adherent over a portion of the left ventricle and the left auricle. The left auricle is equal in size to the other three chambers. It holds approximately 750 c.c. of salt solution. The mitral valve is typically fish mouth in appearance and is partially calcified. The lumen will admit only the tip of the index finger. The left ventricle is definitely hypertrophied and slightly dilated. The papillary muscles, particularly about the mitral valve, are greatly thickened. The aortic orifice is stenotic from firm, old adhesions between neighboring leaflets. Very little calcium is deposited

Fig. 4. The heart as a whole after fixation and some distortion. The portion above the line represents the left auricle and is almost as large as the other chambers combined.

here. A few friable, recent, reddish small vegetations are present along the free margins of two aortic cusps. The right ventricle is markedly hypertrophied, and is slightly dilated. The tricuspid valve is definitely narrowed and shows a few vegetations. There is no ante-mortem clot in any of the chambers. The heart as a whole weighs 650 grams (Fig. 4).

There is about 500 c.c. of fluid in the right pleural cavity. The right middle and lower lobes are completely atelectatic, fibrosed and show a relative increase in the number of blood vessels and bronchi. The bronchi show an excess of mucohemorrhagic exudate. The right upper lobe is air-containing. The left lung shows two small infarcts in the periphery of the lower lobe. The liver is the typical picture of cardiac cirrhosis. Microscopically the musculature of the left auricle is fibrosed and the intima shows calcification.

Anatomical Diagnosis.

(1) Acute, superimposed on a chronic endocarditis of the aortic, mitral and tricuspid valves.

(2) Endocardial sclerosis with calcification of the left auricle.

(3) Cardiac hypertrophy and dilatation, especially of the left auricle and right ventricle.

(4) Chronic, circumscribed adhesive pericarditis.

(5) Pleuro-pericardial adhesions—fibrous.

(6) Right hydrothorax.

(7) Atelectasis of the right middle and lower lobes.

A comparison of this case with those in the literature (Table 1) shows a striking similarity throughout. The oldest case was in a man aged sixty, the youngest in a man aged eighteen. The average age is 34.4. Nine cases are in females and 6 are in males. Rheumatic fever was definitely the etiological factor in 10 cases. The mitral valve showed changes in every case, varying from a thickening (4 cases) to stenosis (7 cases), and incompetency (4 cases). The left auricle was definitely fibrosed in 9 cases and varied in its capacity from 250 to 1,080 c.c. The layers of the pericardium were adherent in every case and in a large majority of the cases the adhesions were present over the left auricle only. Therefore all the cases showed lesions most marked in the region of the left auricle. It would seem that at one time or other a well-marked carditis had been present, the brunt of which, for some unknown reason was sustained by the left auricle.

Symptoms and Physical Signs

D. Evans Bedford in his review states that the symptoms are those which we associate with mitral stenosis and adherent pericardium. I quote him:

"In the earlier stages there are no characteristic physical signs, and the diagnosis is only possible by radioscopic examination. When the left auricle approaches the right chest wall, however, the signs are suggestive. There is a variable area of dullness to the right of the sternum and in the right axilla. Forcible systolic pulsation is palpable to the right of the sternum and in the right axilla at the level of the 4th and 5th interspaces, due to regurgitation through

TABLE I

SUMMARY OF PREVIOUSLY REPORTED CASES

	Author	Age at Death	Sex	Probable Etiology	Mitral	Size of Mitral Orifice	Aortic	Tricuspid	Size of Auricle	Fibrosis of Left Auricle	Pericardium	Remarks
1	Owen and Fenton[16]	40	F	Rheumatic fever	Thickened edges	Admitted 4 fingers	Normal	Normal	30 ounces	Not stated	Adhesions over left auricle	Tapped
2	Owen[17]	27	F	Question-able	Thickened and puckered	Easily admitted 3 fingers	Not stated	Not stated	Equal to 2 closed fists	Not stated	Fibrous adhesions over left auricle	St. Bartholomew's Hospital case
3	Jones[10]	60	M	No history of an acute illness	Little thickened toward free border	Not stated	Normal	Normal	Would contain other three chambers	Not stated	Generally adherent	Hemorrhagic pericarditis; three circumscribed areas, one much older than other two
4	Lutembacher[12]	51	F	Rheumatism at 18	Sclerosed and rigid; incompetent	Admits 2 fingers	Normal	Normal	400 c.c.	Marked; only traces of muscle left	Adherent over upper left auricle	Ulcerating tuberculosis, right base
5	Lutembacher[13]	18	M	Rheumatic fever at 6 and 8	Incompetent	Admits about 2 fingers	Not stated	Not stated	250 c.c.	Fibrosis and hyalinization	Adherent over upper pole of left auricle	Branch of coronary to left auricle obliterated by a thrombus
6	Lutembacher[13]	20	M	No history of rheumatic fever	Incompetent	Admits 4 fingers	Normal	Orifice a little dilated	500 c.c.	Marked sclerosis; thin, white and fibrous	Adherent all over	
7	Shaw[20]	28	F	Rheumatic fever at 12	Stenosed	Barely admits tips of 2 fingers	Not stated	Not stated	30 ounces	Not stated	Generally adherent	Bronchi and trachea compressed and displaced to right
8	Schott[19]	53	M	Rheumatic fever	Stenosed	—	Not stated	Not stated	Enormous enlargement	Not stated	Not stated	
9	Lewis	40	M	Rheumatic fever at 20. Repeated	Thickened and shrunken	Admitted tips of 3 fingers	Normal	Incompetent	1.5 pints	Upper part of left auricle devoid of muscle tissue	Universally adherent	Quoted by Bramwell and Duguid[3]
10	Lewis	29	F	Chorea at 5 and 10	Stenosed	—	Not stated	Enlarged and thickened	Greatly dilated	Left auricular wall not much thicker than paper	Universally adherent by soft adhesions	Quoted by Bramwell and Duguid[3]
11	Cowan	38	F	Rheumatic fever—several attacks	Stenosed	Button-hole	Chronic endocarditis	Thickened and stenosed	Equal to 2 closed fists	Marked sclerosis of auricular wall	A few scattered patches	Quoted by Bramwell and Duguid.[3] Recent acute vegetations on all three valves

TABLE I (*Cont.*)
SUMMARY OF PREVIOUSLY REPORTED CASES

	Author	Age at Death	Sex	Probable Etiology	Mitral	Size of Mitral Orifice	Aortic	Tricuspid	Size of Auricle	Fibrosis of Left Auricle	Pericardium	Remarks
12	Bramwell and Duguid[3]	25	M	Rheumatic fever at 10	Incompetent	Admits tips of 5 fingers	Normal	Normal	1,080 c.c.	Fibrosed	Adherent only over left auricle	Dilatation of left auricle, most marked in right wall
13	East[4]	38	F	Rheumatic fever at 16 with frequent attacks	Marked stenosis	Slight crescentic slit	Thickened but competent	Much dilated	1.5 pints	Marked fibrosis	Obliterated everywhere	
14	Emanuel[5]	48	F	?rheumatic; growing pains in childhood	Stenosed	Fish mouth	Not stated	Dilated	40 ounces	Not stated	Dense adhesions over a triangular portion left auricle	Tapped
15	Steel	31	F	Rheumatic fever at 16 and 27	Stenosed	Fish mouth	Chronic endocarditis	Fused and thickened	750 c.c.	Fibrosed and partially calcified	Adherent over left auricle and ventricle	

the mitral valve. In almost all recorded cases, auricular fibrillation has been present, and therefore pre-systolic pulsation is not to be expected, though it seems doubtful whether the thin fibrous sac which constitutes the auricle could in any case cause a perceptible impulse by itself.

"There may be a systolic thrill in the right axilla (this case was not proved by post-mortem) and as in Emanuel's case. The heart sounds are audible over the pulsation in the right axilla and the systolic murmur is louder there than at the apex. In all cases that I have seen there has been diminished air entry and some degree of dullness on percussion at the right base posteriorly. These signs may suggest pleural effusion, and in two recorded instances, the left auricle was actually punctured during attempted paracentesis. In both the present cases and in some others that I have seen, congestive heart failure was absent. When there is no engorgement or noticeable pulsation of the jugular veins and no liver pulsation the exclusion of tricuspid regurgitation and extreme dilatation of the right auricle is easy. It is doubtful whether or not the right auricle ever causes pulsation in the right axilla. Dullness to the right of the sternum may suggest pericardial effusion, but this should be excluded when there is forceful pulsation and a loud murmur or thrill over the dull area."

ROENTGENOLOGICAL DIAGNOSIS

In the presence of a mitral lesion the first chamber to undergo a change is the left auricle. This change early consists of a hypertrophy and dilatation—mainly the latter. As back pressure increases in the lesser circulation the right ventricle becomes enlarged. In the normal this chamber is entirely anterior, impinging anteriorly against the sternum and inferiorly against the diaphragm, and forming no part of the cardiac silhouette in the posteroanterior view. Therefore when it enlarges it meets with resistance anteriorly and inferiorly and finds room for itself by rotating the heart, which rotation, when viewed from the apex

takes place in a clockwise direction. The result of this rotation which interests us at present is its effect on the position of the left auricle. This chamber is normally posterior and does not form a part of the left cardiac silhouette. With the above-mentioned rotation the left auricle becomes even more posterior and definitely more to the right. In its early enlargement the auricle finds room posteriorly. It will then be seen in the first oblique position as a rounded shadow encroaching upon the mid-portion of the retrocardiac space (Fig. 5). With further enlargement the mid-portion of this space will be entirely obliterated. The upper portion of the retrocardiac space will remain of normal radiability and the lower portion will be characteristically a triangular shadow of normal radiability. The left auricle meets with obstruction anteriorly and to the left by the strong left ventricle. Posteriorly are

Fig. 5. First oblique view showing the rounded shadow of the left auricle impinging on the mid-portion of the retrocardiac space (arrow).

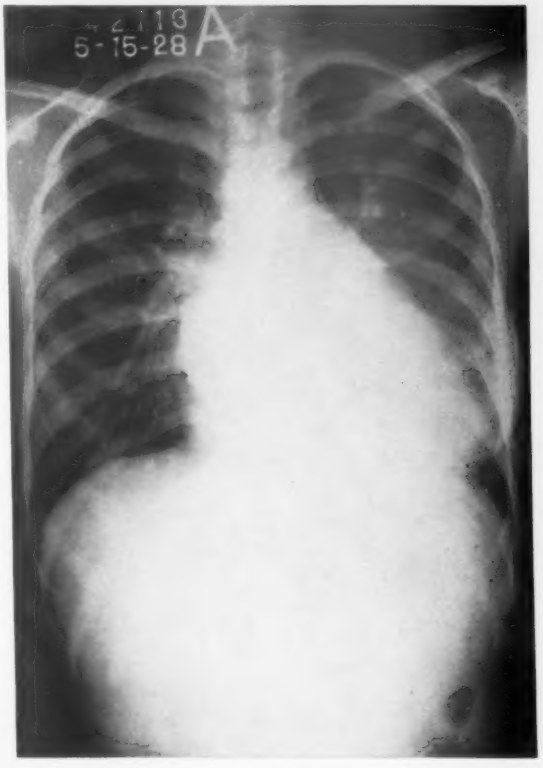

Fig. 6. The shadow of the left auricle (arrow) shows through the less dense right auricle.

the spine and aorta. Therefore it takes the path of least resistance—namely, to the right. This is enhanced by the above-mentioned rotation. In the posteroanterior view the left auricle will be seen first as a shadow of increased density through the shadow of the less dense right auricle (Fig. 6). Later its edge protrudes slightly beyond the border of the right auricle and produces a niche between the two (Fig. 7). The right lower cardiac arch is now divided into two arches —the upper due to the left auricle and the lower to the right. As enlargement of the left auricle becomes greater and greater the upper shadow extends more and more until it forms the right cardiac border (Fig. 8).

DIFFERENTIAL DIAGNOSIS

Given this final silhouette, there are several lesions producing a similar outline which must be differentiated. The first question naturally arising in one's mind is

Fig. 7. The left auricle extends beyond the right auricle forming two arches in the lower right silhouette which are separated by a niche (arrow).

whether or not the right auricle could produce the shadow. The greatest right median

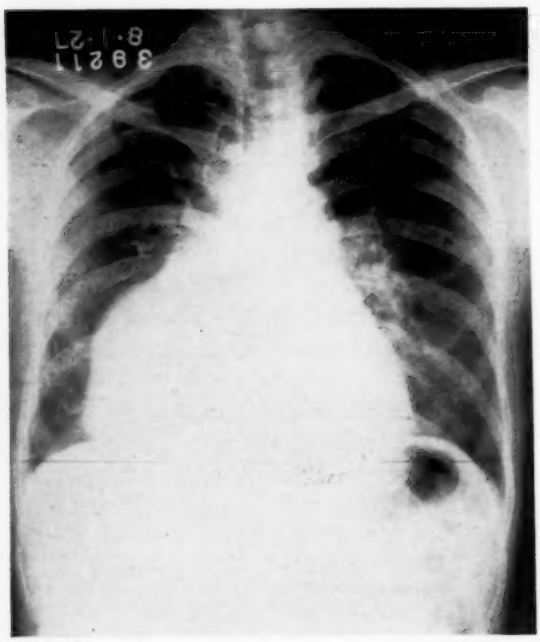

Fig. 8. The left auricle forms practically the entire right silhouette.

distance is considerably above the diaphragm and hence is higher than the right auricle. The shadow is not anterior in the region of the right auricle, but is posterior and obliterates the retrocardiac space. If the right auricle were to reach such a size we would expect a prominent superior vena

Encapsulated pericardial fluid is difficult to differentiate. Figure 9 represents a case cava and hence an enlarged cardiac pedicle. The opposite is true—the superior vena cava is not seen and the cardiac pedicle is

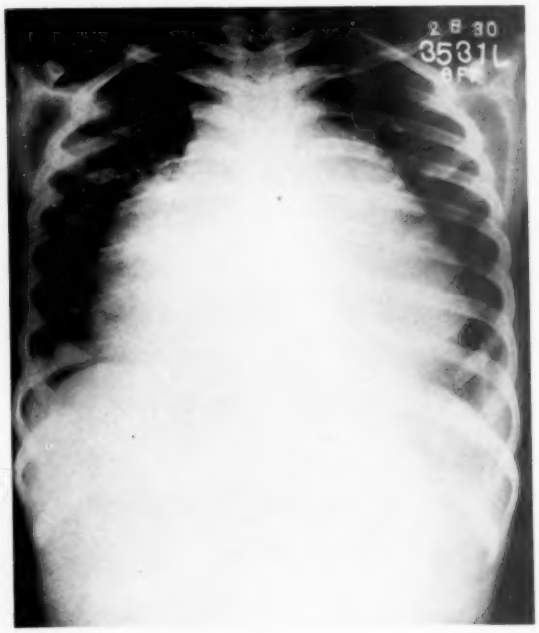

Fig. 9. Encapsulated pericardial fluid forming the right cardiac border.

small. The left silhouette is consistent with a mitral lesion and since this is practically always associated with an enlargement of the left auricle, and since tracing the development of this silhouette shows that the left auricle takes exactly this position, no difficulty should be experienced in ruling out the right auricle and establishing the true cause of the right silhouette.

occurring in a child of twelve with a history of repeated attacks of rheumatic fever and clinically proved pericarditis with effusion. In this case a pancarditis was present. The left silhouette suggests a mitral lesion. The

bulging of the right silhouette was due to a localized pericardial effusion and was mistaken for an enlarged left auricle. However, the history of a previous pericardial effusion, the widened cardiac pedicle, the increased superior vena cava and the age of the patient should have guarded against interpreting the shadow as a large left auricle. This case probably represents the acute stage of inflammatory diverticulum of the pericardium, a lesion which is chronic and presents a characteristic hexagonal silhouette.

Aneurysms of the ascending aorta are usually associated with other roentgen signs of lues of the aorta. Their silhouette is usually more rounded and more sharply defined and their radius is smaller. Mediastinal tumors are scarcely to be confused. Lateral views of the thorax will usually differentiate fluid encapsulated in the interlobar septum and mediastinum.

SUMMARY

A proved case of marked dilatation of the left auricle is described and the findings in 14 other cases from the literature are reviewed. Rheumatic fever is the outstanding etiological factor. Changes in the architecture of the mitral valve were present in every case. The pericardium showed adhesions in every case save one, where its presence or absence was not mentioned. The cases prove that when the left auricle undergoes enlargement it finds its way to the right and may form the entire right cardiac border in the posteroanterior view. Even with such great dilatation as seen in this case the left auricular appendage only was in the left cardiac silhouette. Roentgen examination is important, for it is the only method by which an early diagnosis can be made. In the later stages, when the physical findings are suggestive, the roentgen findings are characteristic.

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ROENTGENOLOGIC STUDIES OF THE MUCOUS MEMBRANE AS AN AID IN THE DIAGNOSIS OF PEPTIC ULCER

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SOME twenty-five years ago, Krehl presented the conception—unique at that time— that disease should not be studied solely from the standpoint of morphology but that efforts must be made to detect it on the basis of disturbed function. This was so reasonable on its face that it led to a prompt alteration of viewpoint—a change almost too sudden to be of practical value. It was a stimulating and far-reaching revolt, that of Krehl, and nobody will deny that he initiated an era of great thinking that will ever endure, an era that has already yielded much of value with regard to diseases of the kidney and heart and promises to give us additional knowledge in other fields of diagnosis. Nevertheless, it cannot be gainsaid that the extremity of the reaction that developed after Krehl's recommendation and the growing tendency to minimize the important rôle of morphologic changes in an organ proper in the intrepretation of disease more than offset the general usefulness of an understanding of the organ's functional disturbance.

With regard to roentgenology, the earliest workers, falling in line with the general trend, directed their attention chiefly to disturbed function. With the exception of large defects clearly indicating disease of an organ, they interpreted the signs of disease on the basis of disordered function. Holzknecht even went so far as to indicate certain functional gastric disturbances as a guide to the roentgen diagnosis of early cancer of the stomach. It was not entirely realized at first that confusion must inevitably result if the roentgen interpretation of pathology were based upon functional disturbances. Experience, though, soon brought about the realization that functional disturbances do not always keep pace with pathologic changes in an organ, and vice versa. The well-known clinical axiom was recalled that feeling sick does not mean being sick, and being sick does not mean feeling sick. Nausea, it was recognized, might be due to purely functional headache, gall-bladder or renal disease, or it might be a manifestation of a functional secretory disturbance of the stomach. Also, there may be extensive kidney or stomach disease without nausea. The direct visualization of pathologic changes in the gastrointestinal tract gained the upper hand, a desired result achieved largely through the painstaking efforts of Cole and his pupils, Gerber, George and Leonard, in this country, and of Haudek, Chaoul, Forssell, and Åkerlund abroad. Thus was the interpretation of direct morphologic changes restored to its proper place.

It should be clearly stated, however, that this does not imply that the utilization of the functional roentgen signs is unimportant. Any evidence of disturbed function such as disorganized peristalsis or alteration in shape of the organ as a result of disturbed function must be most carefully noted. The roentgen signs pointing to morphologic changes and which point directly to the seat of the lesion by far outweigh in diagnostic importance such roentgen evidence as is brought about by functional disturbance caused by a lesion.

Those roentgen signs which demonstrate morphologic changes are termed in roentgen literature "direct signs"; those that are caused by functional disturbance "indirect signs." The direct signs have been

likened (Held and Gray) to objective symptoms, and the indirect to subjective symptoms. Objective findings are persistent unless the lesion heals; subjective symptoms, although due to the identical lesion, may vary a great deal. They may be present at one time and absent at another. In some individuals, the lesion may be present with minor or no subjective symptoms; in others it may give rise to markedly exaggerated symptoms. In other words, that which is true of subjective complaints of a patient is also true of the indirect roentgen signs of the diseased stomach. The indirect roentgen signs or so-called subjective roentgen symptoms, such as disturbed peristalsis, disturbed emptying or transient spasm, may be out of proportion to the existing lesion in the organ depending upon the status or the sensitiveness of the individual or upon the reaction of his vegetative system (vegetative nerves, electrolytes and internal secretion). Subjective roentgen signs in the stomach may exist with the lesion far away from that organ, that is, in the cecum, ileum, diaphragm or in the thoracic organs. In the utilization of the direct or objective roentgen signs, roentgenoscopy and roentgenography alone should and do suffice to establish a diagnosis in the majority of cases. The history serves only as an adjuvant. In the utilization of the indirect or subjective roentgen symptoms, however, the history and other methods of examination, such as studies of secretion, must be called upon to throw light upon the roentgen subjective symptoms.

When evaluating roentgen signs of the gastrointestinal tract in general and of the stomach in particular, it is our habit to pay the greatest attention to the direct or objective roentgen signs, in which case we avoid as much as possible a preliminary history or the employment of additional diagnostic methods. These are pure adjuvants, as stated in the foregoing paragraph. In case, however, that the direct or objective signs are meagre or absent, and subjective or indirect signs predominate, the balance of reliance rests in the history and the findings of other methods of examination.

A recent, very important addition to the direct roentgen signs is the visualization of lesions in the mucous membrane of the stomach in connection with peptic ulcer. This does not imply that the other direct signs and the studies of Cole, Haudek, Chaoul, Forssell and Åkerlund are less important than formerly; it means rather that our diagnostic equipment has been increased.

Since the beginning of the era of roentgen diagnosis of the stomach many observers have from time to time touched upon the value of the direct visualization of the mucous membrane of the diseased organ. Holzknecht especially deserves credit for dwelling often on the importance of this. That was why he advocated a barium suspension instead of the heavy Rieder contrast meal. Lenk and Eisler, his pupils, were the first actually to demonstrate roentgenologically morphologic changes in the mucous membrane and muscularis mucosa in the direct vicinity of peptic ulcer. The subject, however, continued to be more or less enshrouded in mist until Forssell, who had already contributed greatly to our knowledge of the muscular architecture of the stomach, succeeded, after many laborious experimental, clinical and roentgenologic studies of the mucous membrane of the stomach, in obtaining proof of its important rôle in the function of the stomach. Forssell demonstrated beyond doubt that the mucous membrane is possessed of its own motility, mobility and contractility, and that these are brought about by the muscularis mucosa innervated by the Meissner plexus and the ganglion supplying the muscularis mucosa. Prior to that time, changes in shape of the mucous membrane had been attributed entirely to activity of the stomach musculature in general. Forssell separated the entire mucous membrane from the animal and showed that there was motion in the absence of the main muscular

coats. It had been doubted until that time whether the muscularis mucosa alone could influence the activity of the mucous membrane. It had been thought that the strong musculature of the muscularis propria must actually bring about the activity of the mucous membrane. Thorell[1] later succeeded in separating the muscularis propria from the mucous membrane with its muscularis mucosa and thus fully confirmed the work of Forssell. Aschoff has likewise substantiated Forssell's findings on the fresh cadaver.

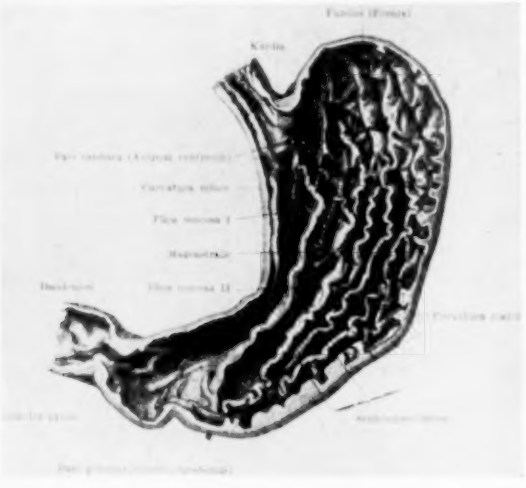


Fig. 1. The mucous membrane of the anterior portion of a stomach at post mortem (after Elze).

Forssell revealed also that the mucous membrane of the stomach as seen on the post-mortem table (Fig. 1) does not fully correspond to its appearance during life. At post mortem, the mucous membrane of the pars media runs in almost parallel folds; in the fornix it runs both parallel and obliquely, and in the pars pylorica it runs in parallel, transverse folds. In the bulbus duodeni or cap its folds are thin and parallel. During life the course of the folds is subject to change, depending on the function of the mucous membrane, upon the activity of the secretory glands, and upon gastric peristalsis (Fig. 2). Respiration with its influence on the mobility of the stomach also alters the course of the folds of the mucous membrane. The pulsation of the heart, the abdominal aorta, and the motions of the diaphragmatic muscles of the left dome of the diaphragm also considerably influence the course of the folds of the mucous membrane, particularly in the fornix but also in the pars media.

The mucous membrane, having its own contractile power by virtue of the muscularis mucosa, and the contractions in turn varying with the degree of filling, it is natural that the shape of the mucous membrane folds will alter considerably. The secretory glands also vary in function, depending on the quality and quantitiy of food ingested as well as upon the psychic state of the individual. If the secretory glands are active in their function, the folds of the mucous membrane vary so that their

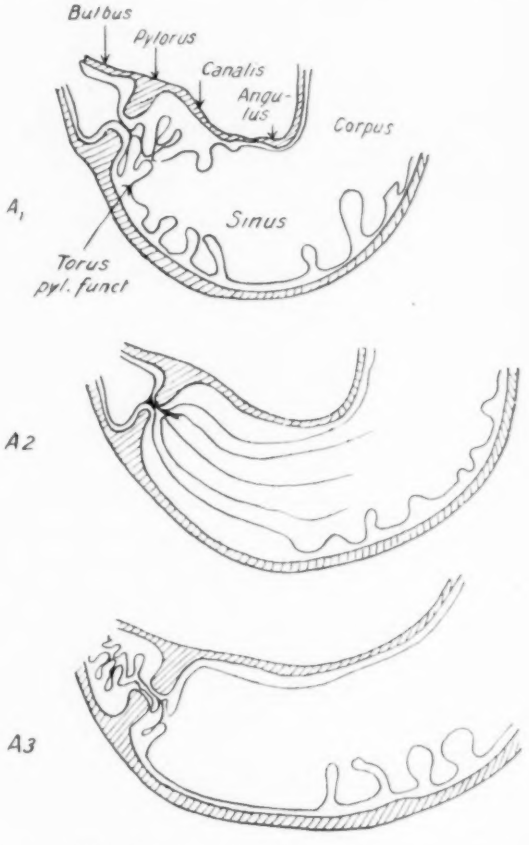


Fig. 2. Showing the changes of the mucous membrane in the pylorus of the living stomach due to contraction (after Forssell).

[1] Thorell, G., *Ztschr. f. ang. Anat.*, 1918, p. 222.

parallelism is lost to a large extent. Folds that run parallel to each other may become narrower in certain parts and wider in others. In some regions, the parallelism is

Fig. 3. The parallelism of the folds of the mucous membrane in the fornix is effaced because the barium meal was thicker than usual.

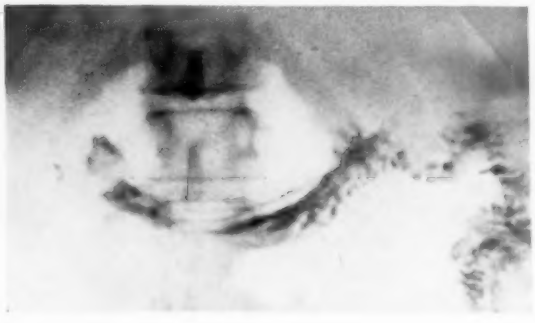
entirely lost due to the presence of contrast food within the meshes of the fold. (Fig. 3). The shape of the mucous membrane may also be influenced by the amount of air that the stomach contains, the quantitiy being abundant during the process of eating and during hyperdigestion. The presence of air alters mainly the course of the folds in the fornix (Fig. 4). In such cases, although the mucous membrane may be normal, its course is altered by the presence of air bubbles plus contrast mixture which appear as light zones on the positive and as dark zones on the negative. Air bubbles may also be present in the first portion of the duodenum and change the appearance of the longitudinal folds, presenting an appearance of small, round light zones on the positive and dark zones on the negative. Very rarely, the entire stomach may be filled with air which, together with the contrast meal, greatly modifies the shape and course of the folds of the mucous membrane without the presence of inherent disease. Regarding the influence of the musculature of the stomach on the mucous membrane folds, it is self-evident that an active stomach musculature bringing about gastric contractions must affect the shape and course of the folds. This is particularly so with the mucous membrane of the greater curvature of the fornix, pars media, and the entire pylorus. The mucous membrane of the lesser curvature, being more or less fixed like the musculature of the lesser curvature, is not much altered in shape as a result of muscular contraction. As a matter of fact, the folds of the mucous membrane of the lesser curvature are very faint as a rule, appearing as thin, parallel lines. This

Fig. 4. Normal stomach after the ingestion of Seidlitz powder. Note the gas that fills not only the pars media and fornix but also causes bubbles in the first portion of the duodenum effacing the mucous membrane.

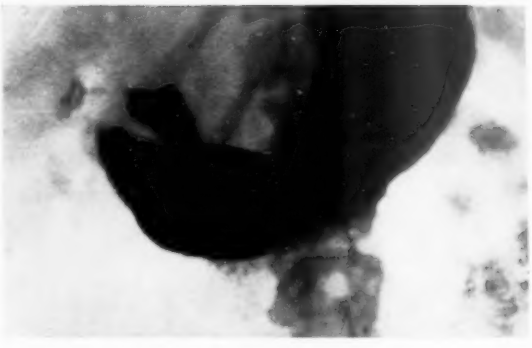
Fig. 5. Normal mucous membrane folds, running in a parallel course in the fornix and pars media.

is very important because if along the course of the lesser curvature there is a distortion of the parallel lines, such distortion is due to alteration in the mucous membrane proper as the result of pathology (ulcer).

The mucous membrane folds on the greater curvature from the fornix to the prepyloric region may stand out very prominently, or they may be flat, depending on the activity of the mucous membrane proper or upon the contractility of the gastric musculature (Figs. 5 and 6). In the fornix the prominence of the folds is due altogether to the activity of the mucous membrane, whereas in the pars media and prepyloric region the prominence of the folds may be due to both the activity of the muscularis mucosa influencing the mucous membrane and to the contractility of the stomach, but usually very much more to the former. In the full stomach, the folds of the mucous membrane may be evidenced on the greater curvature by serrated contractions which, at the fornix, may be so marked as to simulate a defect, and lead one to make an erroneous diagnosis. Such errors have, indeed, been made in the clinic to the alarm of the patient. Exploratory operation is sometimes carried out in these cases owing to a suspicion that the "defect" is due to carcinoma. In the pyloric region proper the activity of the pylorus can convert the parallel folds into very peculiar shapes (Fig. 7). This is the reason why some authors still deny the independent activity of the mucous membrane, stating that in every respect the shape of the mucous membrane depends on the activity of the general gastric musculature. However, it is readily understood that



(*a*)



(*b*)

Fig. 6. Outline of entire mucous membrane from the fornix to pylorus, running in normal parallel folds. Mucous membrane of the duodenum is seen to have an ulcer niche. There is also a pseudo-diverticulum. (*a*) Mucous membrane showing part of the diverticulum filled. (*b*) Taken on the same patient with the full meal, showing adhesions with a pseudo-diverticulum.

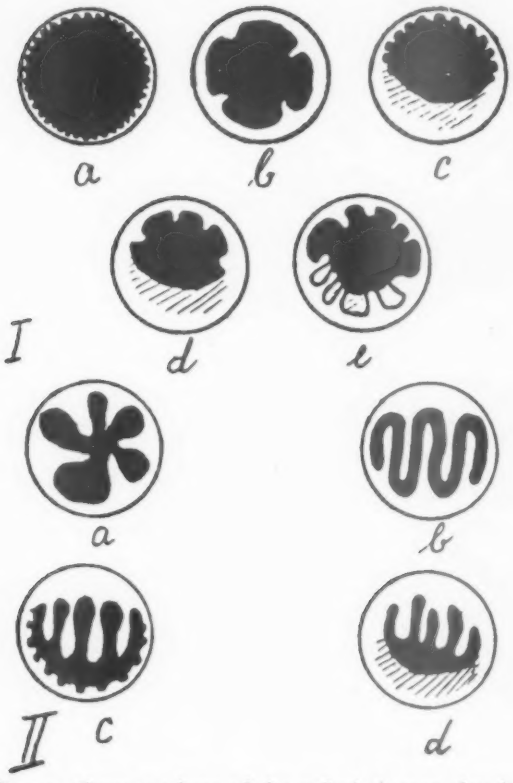


Fig. 7. Cross sections of the pyloric lumen showing contractions of the mucous membrane (after Forssell).

yielding tissue always alters in shape easily under the influence of active pressure from without. That the mucous membrane does alter in shape from such outward pressure is no more proof of its inability to alter in shape independently of such pressure than would the fact that a stomach may alter its shape due to a tumor from without be evidence of its inability to change its shape of its own accord and without external pressure.

METHOD OF VISUALIZING THE MUCOUS MEMBRANE

To study the mucous membrane we must use a meal that will not stimulate gastric secretion in order to exclude the activity of the gastric glands, and it must be one that will if possible not stimulate gastric peristalsis. It must not be voluminous. Otherwise it will fill the stomach excessively and efface the mucous membrane proper. Berg[2] advocates a very thin suspension of barium sulphate in water, 2 or 3 tablespoonsful in 150 or 200 c.c. of water. He cautions rightfully that for the inexperienced observer it is better to use larger quantities of water and somewhat more barium. Berg uses the so-called graded exposure which is obtained with a special apparatus and technique. He first roentgenoscopes, locates the lesion he wishes to photograph, and then takes graded films under compression. He has most vividly demonstrated the value of his method from the physiologic and diagnostic standpoints, but on account of the expense of this apparatus and the extensive amount of time required of the operator in the roentgenoscopic room it is not possible for this ideal method to become universally employed.

Rendich[3] advocates a 50 per cent mucilage of acacia to which an equal quantity by volume of bismuth subcarbonate is added. This mixture is best administered while the patient is in a partially recumbent position (10° inclined) on the roentgenoscopic table, a level teaspoonful being given. A table especially designed for examination of the alimentary tract in the horizontal position is used. Rendich's method is to make the roentgenoscopic examination until the rugae are well delineated without palpation. With this method Rendich made a very valuable contribution to our knowledge of the diagnostic value of a roentgenologic study of the mucous membrane in ulcer, cancer and even gastric catarrh.

The method we have adopted as best accessible to us, and we believe readily accessible to others, is the following:

We give the patient one tablespoonful of barium sulphate in a glass of water. The water must not be too cold or it will stimulate peristalsis. The taste of the mixture may be objectionable to some but if an adjuvant like chocolate is added to give it

[2] Berg, H. H. Röntgenuntersuchungen am Innenrelief des Verdauungskanals. Georg Thieme, Leipzig, 1930.

[3] Rendich, Richard A. The roentgenographic study of the mucosa in normal and pathological states. Am. J. Roentgenol. & Rad. Therapy, 1923, *10*, 526–537.

a more delectable flavor there is the disadvantage of stimulating gastric secretion and causing gastric peristalsis. The patient quickly drinks the mixture of barium sulphate and water, which passes immediately through the stomach into the first portion of the duodenum and often at once into the descending portion of the duodenum. This fills the stomach completely in its various parts and thus permits a visualization of the greater part of the mucous membrane. A large film is then taken of the entire stomach and duodenum. In order to study the individual parts of the mucous membrane with as much exactness as possible, especially in the ulcer-bearing areas, the following procedure is now carried out:

The patient is asked to lie on his right side for 3 to 5 minutes in order to permit the barium to sink into the first portion of the duodenum. Then he is requested to stand and a film is taken in the second oblique position. After that he assumes a horizontal slightly oblique position with the duodenum to the film and the left shoulder to the tube so that another exposure may be obtained. In this way we procure a good outline of the first portion of the duodenum. Following this, the patient lies on his abdomen for a study of the pars media. A rubber ball the size of an orange is placed under the upper part of the abdomen against which the patient presses actively. This separates and distributes the contrast meal throughout the folds of the mucous membrane better than without compression, although at times a like result may be obtained without compression. In an obese individual, where a great layer of fat intervenes between the stomach and the abdomen, compression is absolutely essential. In thin individuals the folds of the mucous membrane in the pars media are seen very often without compression and indeed compression in these individuals may at times distort the mucous membrane too much. We therefore recommend that films be taken with the thin patient on the abdomen without compression. But if a good outline is not obtained, compression should be employed, though not to the degree necessary for a stout individual.

To visualize the course of the mucous membrane in the fornix and in the lower part of the esophagus, a film is taken with the patient standing about 30° obliquely with the left shoulder to the tube. Before taking this film, however, we give the patient another half tablespoonful of barium sulphate in half a glass of water because by this time the barium may have left the fornix. Some advocate contrast paste or barium emulsion for the study of the mucous membrane of this region, but we have found that emulsion or paste coats the fornix and lower part of the esophagus so well that the mucous membrane is entirely effaced. We therefore advocate only the barium suspension.

Finally, a film is taken with the patient lying on his back with the buttocks elevated (Levy-Dorn position).

The foregoing procedure gives information regarding the appearance of the mucous membrane in the different regions of the stomach and has proved to be more conclusive than a roentgenoscopic study. However, we do roentgenoscope the patient for several minutes after the procedure just outlined in order to test the sensitive pressure points in the stomach and duodenum, which we find better located with suspension than when the stomach is more completely filled. By means of the suspension meal it is also possible (as long ago pointed out by Holzknecht) to see roentgenoscopically the manner in which the mixture sinks into an existing niche due to peptic ulcer.

Thus far we have dealt only with the appearance of the normal mucous membrane which, as has been seen, has many deviations for various reasons.

DIAGNOSIS OF ULCER BY MEANS OF MUCOUS MEMBRANE VISUALIZATION

The underlying principle in the diagnosis of an ulcer by a visualization of the mucous membrane with a barium suspension

meal is the detection of alterations in the course of the folds over the ulcer area.

The ulcer-bearing areas of the stomach proper are, as is well known: (1) the posterior wall adjoining and including the lesser curvature; (2) pars media or prepyloric region at the angularis; (3) much more rarely the fornix, and (4) extremely rarely the lower end of the esophagus. An ulcer of the duodenum is generally situated on the posterior wall adjoining the lesser curvature of the first portion of the duodenum and occasionally on the greater curvature. Ulcer is seldom encountered in the descending portion of the duodenum and is extremely rare in the transverse portion. When studying the mucous membrane for ulcer our attention is directed chiefly to the locations enumerated. We must, however, also look closely at the mucous membrane in all other portions of the stomach and duodenum in order to detect associated catarrh or other changes that may exist in the mucous membrane secondary to an ulcer.

In the event of an ulcer in the middle part of the lesser curvature, the folds of the mucous membrane in the direct vicinity of the ulcer instead of running longitudinally parallel become distorted and run horizontally, converging toward the ulcer-bearing area (Fig. 8) as was first pointed out by Lenk and Eisler.

In some cases, not all the longitudinal parallel folds are altered to a horizontal convergence. Some of them retain their horizontal position giving the effect of folds of mucous membrane running in several directions but all converging toward the ulcer proper. This is especially true of the superficial ulcer that penetrates only the mucosa, submucosa, and the muscularis mucosa.

Convergence of the folds of the mucous membrane need not always be due to ulcer. It may sometimes result from gas in the stomach proper or from an overlying transverse colon filled with gas or from an enlarged liver, or it may be caused by pressure of the spleen on the pars media in the region of the greater curvature, or by some alteration in the position of the patient during the examination so that the ray enters obliquely. The experienced observer will easily detect whether or not the distortion and convergence of the folds are the result of an artefact or are due to an ulcer proper. In case the convergence is due to excessive gas the alteration in the mucous membrane folds is seen over larger areas than one would expect in case of ulcer. Whether or not an alteration of the normal appearance of the rugae is caused by tumor can be detected by palpating the abdomen during the course of the examination. If the convergence is due to a change in the position of the patient during the examination the entire outline of the stomach is also changed.

Fig. 8. Note the distortion of the folds of the mucous membrane in the vicinity of the ulcer and their convergence toward the ulcer. No niche is seen (after Berg).

With regard to an ulcer in the region of the

Fig. 9. This is a case of achlorhydria. Repeated studies of the stomach were made which showed no defect, but the stomach is spastic and there is only slight parallelism of the folds approaching the pars media. The folds in the rest of the stomach show no parallelism whatever, indicating catarrh (probably gastritis anacidity).

fornix, where an ulcer is seldom located and where gas and secretions may be excessive, should there be convergence of the folds and a loss of parallelism, a conclusion as to the cause must be guardedly drawn. If there is an ulcer in this region, careful study will reveal a considerable difference between the appearance of the mucous membrane in the area of the ulcer and in other regions.

In case there is a peptic ulcer of the esophagus, although we have had no personal experience with the visualization of the mucous membrane in this region, Berg describes convergence in the direct vicinity of the ulcer and a somewhat ready visualization of a niche.

In the presence of an ulcer of the pylorus, the folds are likewise converged. Here however, the convergence may be obliterated or effaced by the mucous membrane's becoming star- or ring-shaped as a result of pyloric contraction. The convergence of the mucous membrane of the pylorus can only be detected, and its detection become important, if seen when the pylorus is relaxed. During the state of pyloric contraction no conclusions can be drawn from the appearance of the mucous membrane in this region. When the pyloric canal causes marked spasm of the pyloric sphincter interfering with the emptying of the stomach, or when there is considerable stenosis, barium suspension in the pyloric region offers great advantages (Figs. 9 and 10). We see the entire mucous membrane studded with small dots representing deposits of barium in the mucous membrane proper. In case of pyloric stenosis the gross diagnosis is usually made with the contrast meal and it is of the utmost importance that the buttermilk contrast meal be given because stenosing peristalsis and the time of emptying can thus be determined, which would entirely escape us if the suspension alone were given. However, in these cases when a suspension meal is given, the entire pyloric region fills with suspension. Due to the accompanying ex-

Fig. 10. The folds in the pylorus have disappeared due to associated catarrh and pyloric stenosis.

Fig. 11. Showing a niche in the center of the first portion of the duodenum (after Berg).

Fig. 12. Marked folds on the greater curvature in the cardiac portion of the stomach simulating a defect on the film taken with a large buttermilk meal. In this film made after the ingestion of a barium suspension meal, they are apparently due to excessive activity of the mucous membrane in a case of duodenal ulcer.

cessive secretions and the presence of air, bubbles of air with secretions and barium are seen which differentiate the condition from a stenosis due to carcinoma. In some cases of ulcer, we see very marked spasm of the pylorus so that the pylorus is pivot shaped, simulating carcinoma. The barium suspension will make the diagnosis clear by demonstrating the mucous membrane in

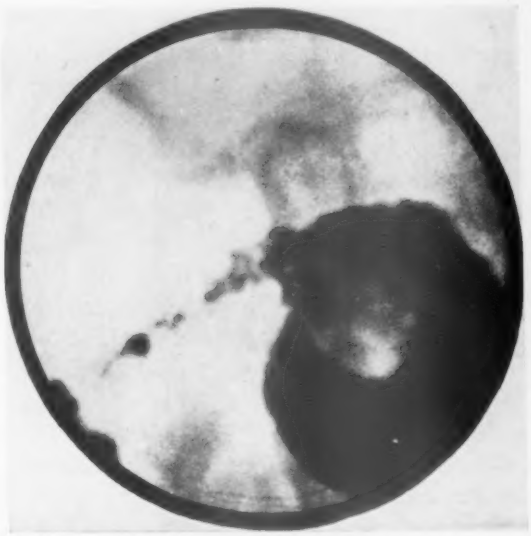


Fig. 13. Showing a defect due to an enlarged gland secondary to duodenal ulcer, pressing on and deforming the pylorus. Note the spastic duodenum and distorted mucous membrane (Berg).

this location. In case of ulcer, the mucous membrane is distorted but is present, whereas in cancer large deposits of barium are seen with hardly any evidence of the mucous membrane.

When there is an ulcer in the first portion of the duodenum, the mucous membrane is usually distorted so that the folds lose their parallelism in the direct vicinity of the ulcer although there is no absolute evidence of convergence (Figs. 11, 12 and 13).

In postoperative jejunal ulcer, Berg likewise mentions marked distortion of the mucous membrane. The visualization of the mucous membrane, although valuable here from the standpoint of the visualization of a niche, is not so valuable from the standpoint of peculiarity of appearance in

the area of the ulcer. Here even a normal mucous membrane has a feathery arrangement without parallel folds. This is also true of the mucous membrane in the second portion of the duodenum.

Appearance of the Mucous Membrane in Areas Adjacent to the Ulcer

Within the immediate vicinity of the ulcer on the lesser curvature, deposits of barium may be seen in the suspension as dots of varying sizes, indicating the existence of an excessive amount of gastric secretion. In marked hypersecretion, the dotted deposits of barium are seen over a larger area of the stomach. When catarrh is present in the distal area (in the pyloric region and sometimes in the duodenum), the parallelism is so distorted that the spaces between the rugae are considerably widened. The folds proper are seen as dark zones in the negative and the thick deposits as light zones. At times there is a snow-flake arrangement. In some cases, in addition to the thickened folds, air bubbles mixed with barium are seen. In those areas of the stomach where there are air bubbles, even if the folds run in irregular courses and there are dense and rather large deposits of barium over the mucous membrane, one is not justified in stating that this area is the seat of catarrh. Even in a normal stomach that contains an excess of air and fluid the barium suspension is irregularly distributed over the mucous membrane. This is well seen in a normal stomach without suspension of barium if the air bag is large. We have demonstrated this by giving a Seidlitz powder to a normal individual after the barium suspension (see Fig. 4). The air bubbles so distorted the mucous membrane that its regularly parallel course was markedly altered. However, in the majority of cases of peptic ulcer during the active stage there is an excessive secretion and even more gas in the stomach than normally. Hence the distortion of the mucous membrane in the vicinity of the ulcer must not be considered as pathognomonic of catarrh unless the irregularity of the folds is actually confined to the distal part of the stomach and to the duodenum. If irregularity and convergence in the folds occur only in the proximal part, it is reasonable to assume that the cause is excessive secretions or gas in the stomach.

In a number of cases, the folds of the mucous membrane of the greater curvature are more prominent than normally and appear in a serrated arrangement. This is not, of necessity, an indication of catarrh, but may mean hypersensitivity of the mucous membrane. Such serrations are also encountered in sub- or anacidity of the stomach, but in these cases the serrations are confined chiefly to the greater curvature of the fornix and the upper part of the pars media. These serrations of the greater curvature are seen very often in chronic appendicitis, in gall-bladder disease and even in normal individuals with hyperactivity of the mucous membrane. Because of their occurrence in so many other diseases than peptic ulcer, the finding of serrations

Fig. 14. Showing a niche on the lesser curvature with convergence of the mucous membrane folds both horizontally and vertically. There is also a niche on the duodenum.

Fig. 15. Same as Figure 14, with mucous membrane of the pars media appearing in spots due to secretions and possibly to catarrh.

of the greater curvature should be regarded really as an adjuvant in the diagnosis of peptic ulcer.

THE DETECTION OF A NICHE BY MEANS OF BARIUM SUSPENSION

Of great importance is the study of the mucous membrane by suspension when a small niche is present, particularly if it is on the posterior wall somewhat away from the lesser curvature, both in the stomach and duodenum. The deposit of barium suspension in a niche may be directly visualized, where it would escape detection if the stomach were entirely filled with a contrast buttermilk meal.

Whereas the detection of a large niche, particularly if situated on the pars media of the stomach or on the lesser curvature of the first portion of the duodenum, is easily detected by means of the contrast buttermilk meal, the small niche almost invariably escapes detection unless barium suspension is employed for the study of the mucous membrane. In Figure 14 two lesions are seen, one on the lesser curvature of the stomach and one in the first portion of the duodenum. In the direct vicinity of the ulcer of the lesser curvature, the mucous membrane converges both horizontally and laterally, and the greater curvature has a serrated appearance. Figure 15 shows spotted deposits of barium throughout the entire pars media, possibly due to catarrh but we believe in this case to excessive secretions. In contrast to these two films is Figure 16 showing the mucous membrane to be markedly distorted with an eaten-out appearance near the lesser curvature, a distortion due to cancer. It may be stated parenthetically that in those cases where the musculature is less involved than the mucous membrane and hence the ulcer defect hardly detectable with the contrast buttermilk meal (as in this case) a study of the mucous membrane by barium suspension will offer a great aid in diagnosis.

The value of the suspension meal in the case of a large niche lies chiefly in determining whether or not the niche is healing. The mere disappearance of a niche, which at one time was thought to be an indica-

Fig. 16. Shows mucous membrane in the pars media distorted and eaten away due to cancer.

tion that the ulcer had healed, has turned out to be inexact. When one can see a niche at one examination and find it entirely absent at another examination two hours later, this certainly cannot be due to the healing of the ulcer. Holland showed in one of his cases that although a lesion had entirely disappeared roentgenologically, at operation a very large niche was found. This illustrates that the niche, unless due to a penetrating ulcer with adhesions to the adjacent organs (traction diverticulum in contradistinction to the non-penetrating pulsion diverticulum, Held and Gray) is probably due to spasm on the lesser curvature or to relaxation of the lesser curvature. Because a suspension meal does not stimulate gastric peristalsis, we are enabled to see the existing niche persistently. Hence the suspension, by revealing a diminution or increase in size, serves as a guide—an absolute guide according to Berg—to the healing of the niche. Berg noticed a gradual diminution in the size of many niches studied by him and a consequent gradual disappearance of the characteristic funnel shape.

The elevated edges around a niche can also be detected better by the suspension meal than with the buttermilk contrast meal. According to Berg, these elevated edges are the result of acute inflammatory changes in the direct vicinity of the ulcer. If this inflammation subsides, the elevation due to the inflammation likewise disappears. Consequently, in many cases Berg states that the reason it is so difficult after a hemorrhage to determine whether or not a lesion exists is because the surrounding elevated edges disappear after the hemorrhage. It is, indeed, a clinical fact that in many cases after hemorrhage due to peptic ulcer the roentgen examination of the stomach and duodenum with a buttermilk contrast meal a few days after the total disappearance of the hemorrhage results usually in negative findings, much to the surprise of the clinician and roentgenologist. The advantage of barium suspension in these cases is that whereas the elevated edges disappear, a fleck (according to Berg) persists, pointing to the seat of the ulcer.

For the detection of the pseudo-diverticulum secondary to duodenal ulcer, as first studied pathologically by Hart and roentgenologically by Åkerlund, the suspension does not offer any great advantage. This may be much better detected by the buttermilk contrast meal than with the suspension meal.

The barium suspension meal, however, offers another advantage in that with this method we are able to detect a lesion on the posterior wall of the duodenum that would otherwise be missed. At times we are able to detect even the kissing type of ulcer by this method.

CONCLUSIONS

The barium suspension meal provides a means whereby we may visualize the mucous membrane in the stomach and duodenum. This visualization of the mucous membrane is important not only for the study of catarrh of the mucous membrane but for the exact location of an ulcer and even for the determination of the healing of an ulcer. We are able to detect in this manner alterations of the mucous membrane in the vicinity of the ulcer proper and also distally to the ulcer. Many small lesions not detectable by the contrast buttermilk meal are discovered when a barium suspension meal is given.

The barium suspension meal can by no means replace the other methods of roentgenologic study in peptic ulcer and it is not claimed that the ulcer can be diagnosed in every case by this method. However, even with our limited experience we feel that because this method has increased the percentage of cases of peptic ulcer diagnosed it deserves a place in our diagnostic roentgenologic armamentarium.

Vol. XXVI, No. 1

THE STUDY OF GALL-BLADDER CONTRACTIONS
AS AN AID IN THE ROENTGEN DIAGNOSIS OF GALL-BLADDER DISEASE*

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APPLICATION of the Graham test to gall-bladder diagnosis has greatly enhanced our knowledge of that organ. However, it seems that a more or less perfunctory adherence to the usual routine technique is not a complete roentgenological examination of the gall-bladder.

FIG. 1. Normal gall-bladder twelve hours after administration of dye.

FIG. 2. Same gall-bladder as in Figure 1, fifteen minutes after ingestion of fat (motor) meal. The vesicle has decreased appreciably in size.

Study of gall-bladder contraction is a very important element in the diagnosis of gall-bladder disease. While some observers are at present not ready to concede the existence of expulsive contractions,[1] and others frankly deny that such a phenomenon occurs, it appears that accumulating experimental and clinical evidence not only establishes the fact of gall-bladder contraction,[2,3] but ascribes to it an importance in diagnosis which is invaluable to the accuracy and delicacy of cholecystography.[4] Active contraction is an essential element of gall-bladder function; for only by this mechanism does the gall-bladder empty itself normally.

It is impracticable to establish an arbitrary limit of time within which a normally distended vesicle should completely empty itself after feeding. In most cases this probably takes place within five or six hours. Yet frequently we see complete emptying within an hour, and, occasionally, a normal gall-bladder may not contract fully in twelve hours.

Thus, it is unlike the stomach, in which a

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50 per cent residue at six hours is definite evidence of obstruction. Usually, however, emptying of the gall-bladder is parallel with gastric and intestinal activity. It is therefore unsound to conclude that a particular gall-bladder is diseased because its shadow is seen on the cholecystogram an hour or more after eating.

Functional disturbances may greatly retard emptying of the gall-bladder. Moreover, the latter is sensitive to reflex stimulation from other digestive organs.

It may be well to recall that the sympathetic innervation of the gall-bladder and liver is the same as that of the stomach, being derived from the semilunar ganglion, which receives connector fibers from the fifth to ninth thoracics. Parasympathetic innervation by the vagus is likewise common to gall-bladder, liver and stomach.[5]

Not infrequently, we have observed during the course of contraction of a gall-bladder, a sudden increase in the size of the vesicle, accompanied by nausea and vomiting (Figs. 1, 2 and 3). This syndrome typifies the response of the gall-bladder to reflex disturbance and appears to be due to a concurrence of two factors: first, a visceromotor reflex effected through the vagus and sympathetics, causing a partial relaxation of tonus of the muscular tunic of the gall-bladder; second, a variable degree of pylorospasm with contraction of the common duct sphincter, causing bile from the liver to enter the gall-bladder instead of the duodenum. Thus, sudden increase in size of gall-bladder shadow, associated with nausea and vomiting, point to reflex disturbance, rather than intrinsic disease.

In these cases the ingestion of more fat (perhaps in different form), frequently excites the vesicle to resume activity (Fig. 4). When continued stimulation elicits no further contraction, the cause is to be sought in the gall-bladder itself.

Fig. 3. Same gall-bladder as in Figures 1 and 2, about one hour later showing an increase in size. There were associated nausea and vomiting. This syndrome typifies the response of the gall-bladder to reflex disturbance.

Fig. 4. Same gall-bladder as in Figures 1, 2 and 3, after administration of another fat meal showing that the vesicle has resumed activity. Complete contraction and emptying were obtained in this case.

GOOD FILLING
SLOW EMPTYING-DUE TO

REFLEX DISTURBANCE	GALL-BLADDER DISEASE	IMPROPER FOOD STIMULATION
(Accompanied by nausea and vomiting.) Further stimulation causes further contraction to complete emptying.		Ingestion of fat causes contraction and emptying.

CHOLECYSTITIS	STONES	PERICHOLECYSTITIS
No contractions seen under roentgenoscope.	Active contractions seen under roentgenoscope. Therefore failure to empty is not due to diseased muscularis. Stones must be suspected. Change of roentgenographic technique may render them visible.	(Due to disease of neighboring viscera.) Active contractions seen under roentgenoscope. Fixation to diseased viscus demonstrated.

FIG. 5. Chart showing the differentiation of the causes of slow emptying of the gall-bladder.

On the basis of the commonly accepted criteria of the Graham test, even diseased gall-bladders may appear to be normal. To make no further search into the activity of the vesicle, such as may be revealed by roentgenoscopic examination, is to ignore that evidence which deals directly with the functional state of the gall-bladder.

FIG. 6. Cholecystogram of a normal gall-bladder in contraction, showing the convoluted portion of the cystic duct (Heister's valve), and the remainder of the cystic duct and common duct.

In many cases of gall-bladder disease, good shadows may be obtained on the cholecystograms, and in each instance the shadow may disappear at some variable period after a fat meal, this interval of time, in itself, having no definite diagnostic significance. The inconstancy and variability of such findings tend to confuse, rather than clarify the diagnosis.

We have long since found it necessary to seek other information concerning the gall-bladder, in addition to what is revealed by routine cholecystography. On the basis of these determinations we have attempted to formulate an approach to the differentiation of the various factors which may cause slow emptying of the gall-bladder.

Reference to Figure 5 shows the three main causes of slow or improper emptying.

Reflex inhibition (as from gastric unrest) is usually associated with nausea and vomiting and may be overcome by the administration of more fat, either immediately or after a brief rest.

In the presence of cholecystitis, no contractions are seen under the roentgenoscope, and the further ingestion of fat-foods causes no further reduction in size; or the reduction in size is so very slight as to be entirely out of proportion to the amount of stimulation.

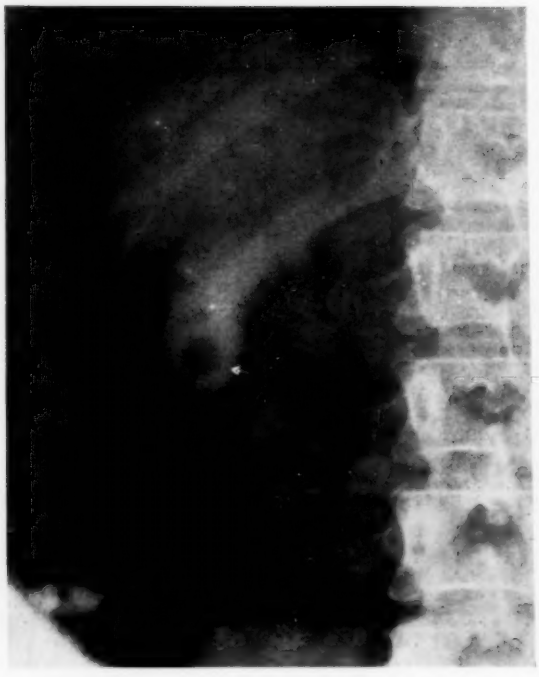

Fig. 7. Cholecystogram showing gall-bladder at rest. Note the stone at the fundus (arrow).

Fig. 8. Same case as in Figure 7, fifteen minutes after ingestion of fat (motor) meal. The gall-bladder is actively contracting as may be seen by the tapering of the fundus. The stone (arrow) has been pushed to the neck of the vesicle, partially occluding the cystic duct.

Stones may cause slow emptying of the gall-bladder. In such cases, if there is no advanced disease of the vesicle itself, active contractions will be seen under the roentgenoscope.

In many cases a single stone may be moved about in the gall-bladder by activity of its muscularis, until it is forced against the convoluted cystic duct (Fig. 6). Here, it may act as a ball valve, and prevent emptying (Figs. 7 and 8).

Therefore, a well visualized gall-bladder which empties itself slowly, but still reveals an active muscular tunic roentgenoscopically, must be suspected of containing stones even though they are not visible. Often there is too much dye in the gall-bladder to allow visualization of negative shadows. By changing roentgenographic technique, or by waiting until some of the dye has passed out of the vesicle, these stones may usually be demonstrated (Figs. 9 and 10).

Movable stones are not likely to interfere with filling of the gall-bladder. They are very apt to retard emptying of the gall-bladder. We do not concur in the hypothesis advanced in the early days of the Graham test, that one of the *chief* causes for non-visualization of the gall-bladder was occlusion of the cystic duct. Of course, this factor is operable in some cases. Usually, however, non-filling of the vesicle is due, not to a physical obstruction of the duct, but rather to a functional deficiency of the concentrating and contracting mechanism of the gall-bladder.

Slight or moderate contraction of the gall-bladder after a fat meal is not sufficient proof that stones are absent. Cholecystograms should show the gall-bladder shadow reduced to a size *too small to contain formed calculi*.

Improper emptying of the vesicle may be due to interference with its contracting mechanism by adhesions to a diseased neighboring viscus. In this type of case we find material assistance in our method of

Fig. 9. Cholecystogram of an apparently normal gall-bladder, twelve hours after administration of dye. Because of slow emptying some disturbance was suspected. Active contractions roentgenoscopically eliminated an impaired muscularis as the cause; therefore the presence of stone was suspected.

Fig. 10. Same gall-bladder as in Figure 9, twenty-six hours after ingestion of fat (motor) meal. Note the single small stone. The presence of this stone was definitely suspected before it was demonstrated.

combining cholecystoscopy with the barium meal.[4]

From the foregoing it may be seen that we place considerable emphasis on study of gall-bladder contraction. The reasons for this are obvious: the functions of the gall-bladder are, first, to store and concentrate bile during the intervals of digestion; second, to discharge this bile when needed. The function of concentration is determined by the density of the gall-bladder shadow. The function of contraction is revealed, not only by the decreasing size of the gall-bladder, but also by its cyclic activity as seen under the roentgenoscope.

SUMMARY AND CONCLUSIONS

Clinical and experimental evidence establishes the phenomenon of contraction as a definite muscular function of the gall-bladder; and study of gall-bladder contraction is essential to the complete roentgen examination of the gall-bladder.

There does not appear to be a definite time limit for the emptying of a normally distended vesicle. This, however, is usually parallel with gastric motility.

Delayed emptying of a well-filled gall-bladder may be due to reflex disturbance, improper food stimulation or gall-bladder disease. The etiological factor in a given case can usually be determined by combining the roentgenologic evidence with careful roentgenoscopic study.

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GALLSTONE OBSTRUCTION OF THE DUODENUM*

WITH SINUS BETWEEN GALL-BLADDER AND DUODENAL BULB

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THE patient walked into the office unaided after an automobile ride of sixty miles with his physician who gave the following history of the case:

Mr. C. T., a farmer, aged eighty, had been well, fat and vigorous until seven weeks ago when he was taken suddenly with an agonizing abdominal pain. On the doctor's arrival he was in collapse with chills and sweating. A half a grain of morphine relieved him and on the following day he sat up several times. He was kept in bed for a week on a liquid diet during which time he ran a low fever and showed a definite jaundice. The abdomen remained somewhat distended but there was no nausea, no vomiting, no constipation.

He got about gradually and made little complaint except for a persistent discomfort and soreness below the ribs on the right side. But by the end of about three weeks he began to vomit and became progressively worse, losing rapidly in weight and strength. For a week preceding the roentgen examination he had been vomiting several times daily, a dark greenish liquid which, however, had no fecal odor. During this week he had had no evacuation of the bowels except by enema and for a number of days the enemas were returned unchanged.

No cathartics had been given because of the signs of intestinal obstruction. A glucose solution had been given intravenously the night before and repeated on the morning of the journey.

Physical examination preceding the roentgen examination showed a moderate distention and mild rigidity of the abdomen. He did not complain of pain and was only slightly tender on palpation.

The roentgen and laboratory examinations were then carried out and reported to the attending physician as follows:

Roentgen Examination.

Chest: The roentgenoscopic examination of the chest was negative.

Abdomen: Before the administration of the barium mixture, a plate was made of the abdominal and pelvic areas with the patient lying prone. An extensive osteo-arthritis of the spine was present. The liver appeared small. In the region of the gall-bladder, a small area of increased density was observed, but no definite gall-bladder or gallstone outline.

Gastrointestinal Tract: The barium mixture was given and the patient studied by screen and films. There were no filling defects or contractures of the stomach itself to indicate ulcer or cancer. The little barium passed through the pylorus and outlined faintly a marked distention of the duodenal loop. The greatest dilatation of the duodenum was just anterior to the duodenojejunal flexure where the barium came to an abrupt end. The barium also entered and outlined a pocket communicating with the bulb of the duodenum.

After the lapse of three hours, additional films were made of the stomach. More barium had passed into the arc of the duodenum and showed more clearly a dilated duodenum, especially the second ascending portion. This still terminated abruptly at the duodenojejunal flexure. At this point the barium was displaced by what appeared to be a large, nearly radiotransparent calculus. Serial plates showed no change in its size or position. It remained faintly outlined by partly surrounding barium, constituting a negative image.

The accessory pocket communicating with the bulb appeared to be the gall-bladder. The barium also partially filled the cystic duct and the common duct and extended into many fine branches of the hepatic ducts. A stereoscopic set of plates was made in the prone position, showing this distribution of the barium.

On the following day, the patient was brought in for further roentgen study. A stereoscopic set of plates was made of the abdomen with the patient lying prone and another with the patient lying supine. Films were also made in the upright position.

The stomach was partially empty owing to the continued vomiting. Only traces of barium had passed beyond the point of obstruction at the duodenojejunal flexure. At this point, there was the outline of what proved to be a very large gallstone.

* Read at the Thirty-first Annual Meeting, American Roentgen Ray Society, West Baden, Ind., Sept. 23–26, 1930.

The common duct, some of the hepatic ducts, the cystic duct and what we interpreted to be the gall-bladder, were outlined to a greater or less extent by barium. The communication between the gall-bladder and the duodenal bulb was discernible because of the partial emptying of the stomach.

When the patient lay on his back there was a partial emptying of the accessory pocket or gall-bladder. The common duct and hepatic ducts remained filled. In the standing position, however, there was apparently a complete emptying of the gall-bladder, although the common duct and some of the hepatic ducts remained outlined. The duodenal bulb showed also a recession of the barium but no diminution in the size of the outline which we interpreted to be a large gallstone.

Laboratory Findings.

Blood: This showed red and white counts which were within normal limits. There was quite evidently a concentration of the blood, doubtless due to the fact that there was an obstruction at the duodenum which would prevent the normal absorption of fluids. No leucocytosis was present.

Urine: One sample of urine was examined. This showed a trace of albumin and both hyaline and granular casts. An excess of bile was present.

Gastric Contents: A Rehfuss stomach tube was passed and an effort made to obtain the stomach contents. The patient, however, vomited profusely a turbid, very dark greenish material. Macroscopically, this was regurgitated duodenal fluid containing large quantities of bile and mucus. No fecal odor was present. The test for occult blood was positive.

Diagnosis. The interpretation of the roentgen findings have been given largely in our previous description. Our final conclusions, from the history of the case and the general examination, were that the patient had a large gallstone, which ulcerated through the gall-bladder into the duodenal bulb and lodged just anterior to the duodenojejunal flexure. In the present case, the gallstone seems to have been of very large caliber, sufficient to bring about an obstruction of the duodenum.

Inflammatory exudate evidently prevented any escape of material from the gall-bladder or duodenum during the passage of gallstones. A large communicating sinus remained, through which the barium mixture passed, filling both gall-bladder and common duct with a distribution in some of the hepatic ducts.

Only traces of barium passed beyond the obstruction in the duodenum at the end of twenty-four hours. The continued vomiting of the patient had partially emptied the stomach; however, fully 50 per cent of the barium remained.

Operative Record. Operation was performed on the following day. A large gallstone was found which was much broken in removal. This relieved the obstruction. The pyloric end of the stomach, gall-bladder and duodenum were buried in plastic exudate and were left undisturbed. The patient did well for two days and then failed, dying on the fourth day after operation. A post-mortem examination was not permitted.

Although autopsy was denied the diagnosis was proved by the finding of the large gallstone. Such a stone could pass into the duodenum only by rupture of the gall-bladder and the path of the stone is clearly shown on the stereoscopic films.

The delineation of the hepatic ducts as well as the common duct by the barium mixture is the most striking feature of the examination. Where the barium went, stomach contents had also repeatedly gone before. Stomach contents must have been mixed with duodenal and pancreatic secretions. During vomiting there must have been considerable pressure forcing such material into the finer biliary ducts where in fact the barium is seen to have penetrated. A hepatitis was inevitable. It is doubtful if barium could add to this effect. Notwithstanding this serious, probably fatal, complication, the patient's condition after duodenal obstruction is very much better than after obstruction of the jejunum or ileum. The usual roentgen signs of acute small intestinal obstruction are of course absent. We see in Figure 1 what happens to the bile also when the common duct is occluded by stone. When the gall-bladder is infected we can wonder that abscess of the liver is not more common. If perforations of the stomach, duodenum or gall-bladder could be foreseen then a soluble, mildly antiseptic mixture could with ad-

vantage replace the barium mixtures now used in the gastrointestinal examination. An iodized oil would have some advantages but for general use its cost is prohibitive.

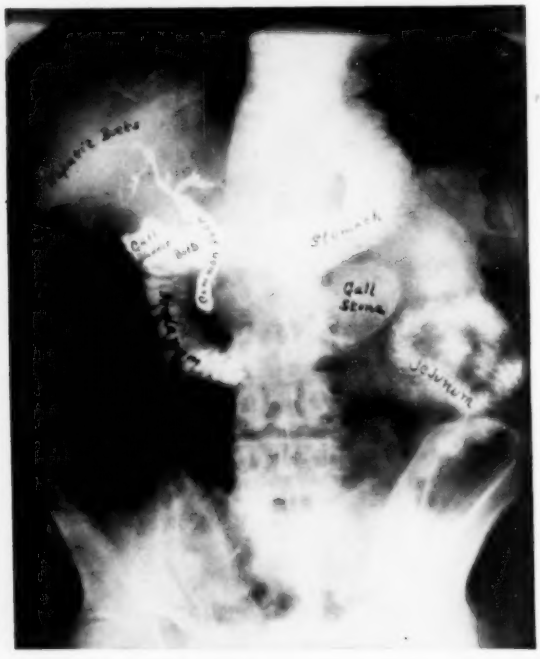

Fig. 1. The duodenum is seen to be obstructed by a large gallstone. A perforation exists between the gall-bladder and the duodenal bulb, allowing barium to pass into the common duct and to outline many of the hepatic ducts.

Carman reports one case of a delineation of the hepatic ducts by barium in his work on the gastrointestinal examination. This resulted from penetrating duodenal ulcer.

In the *Quarterly Cumulative Index* we find in the last eight years, 4 cases reported of gallstone obstruction. The rarer the cases, the greater the proportion reported. During the same period 26 cases of intestinal obstruction below the duodenum were reported. For the world's literature this is not many and we are led to report this case for what it is worth.

1930 P. 389. Duodenum (obstruction)

By gall-stones (P. D. Scofield), *Ann. Surg. 91:* 632–633, April, '30.

Roentgen diagnosis of calculus in duodenum after cholecystoduodenal perforation; biliary ileus 15 days later; autopsy (P. Brocq, P. Brodin & Aime), *Bull. et mem. Soc. nat. de chir. 55:* 1194–1200, Nov. 23, '29.

1930 P. 488. Gall-bladder (calculi)

In duodenum (P. D. Scofield), *Ann. Surg. 91:* 632–633, April, '30.

1929 (5) P. 370. Duodenum (obstruction)

High ileus caused by incarceration of biliary stone; case (S. Mintz), *Arch. f. Verdauungskr. 44:* 382–386, Dec. '28.

1929 (5) P. 469. Gall-bladder (calculi)

False duodenal diverticulum formed by perforation of calculous gall-bladder into wall of duodenum; case (V. Korchov), *Zentralbl. f. Chir. 55:* 2955–2957, Nov. 24, '28.

1929 (5) P. 471. Gall-bladder (roentgenography)

In diagnosis of diseases of duodenum and gall-bladder (F. M. Hodges), *Radiol. Rev. & Chicago M. Rec. 50:* 472–474, Dec. '28.

1929 (6) P. 521. Gall-bladder (calculi)

Causing acute obstruction of small intestine; recovery following operation (G. L. McWhorter), *Arch. Surg. 19:* 915–921, Nov. '29.

1928 P. 397. (3) Gall-Bladder (calculi)

Passage of gallstone into small intestine without pain, followed by obstruction, operation for removal of stone, and death from intestinal paralysis (Fenkner) *Therap. d. Gegenw. 68:* 479, Oct. '27.

1928 (4) P. 439 Gall-Bladder (calculi)

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1927 (1) P. 286. Gall-Bladder (calculi)

Intestinal obstruction from gallstone; "gall stone ileus"; pitfall for practitioner (G. G. Turner), *Post-Grad. M. J. 2:* 65, Feb.; 85, March '27.

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Acute intestinal obstruction from impaction of gallstone (Cabot case 13482), *Boston M. & S. J. 197:* 1061–1064, Dec. 1, '27.

Intestinal obstruction; case due to gallstone; critique of operative technic and sequelae (A. Chenut), *Rev. de chir. 65:* 319–327, '27.

Intestinal obstruction from gall stones; 2 cases (A. Odasso), *Miverva med. 7:* 561–568, May 31, '27.

1927 (2) P. 488. Gall-bladder (perforation)

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Acute perforation or rupture (E. G. Alexander), *Ann. Surg. 86:* 765–770, Nov. '27.

1926 (11) P. 202. Gall-bladder (calculi)

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Intestinal obstructional from gallstones and its spontaneous cure as gallstone was voided (A. Guillemin), *Arch. franco-belges de chir. 28:* 953–962, Nov. '25 (illus.)

Obstruction of small intestine by gallstones; 3

cases without mortality (C. Bennett), *Brit. M. J. 1:* 565–566, March 27, '26.

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1925 (10) P. 357 & 358. Gall-bladder (calculi)

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1925 (10) P. 362. Gall-bladder (surgery)

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2 cases of acute intestinal obstruction due to impaction of gallstones (C. P. G. Wakeley), *Brit. J. Surg. 11:* 380–382, Oct. '23 (illus.)

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1922 (7) P. 276. Gall-bladder (calculi)

Acute ileus produced by large gallstone (C. M. Echols), *Wisconsin M. J. 20:* 474–475, Feb. '22.

Repair of duodenal perforation, cholecystotomy for gallstones (F. W. Bailey), *S. Clinics N. America 2:* 1645–1647, Dec. '22 (illus.).

DISCUSSION

Dr. Leon T. LeWald, New York City. The case is very interesting indeed, and I can add one case of gallstone obstructing the terminal ileum, which has never been reported. I found it at autopsy when I was house surgeon, and in that particular case the stone was just about the same size and had obstructed the terminal ileum. A correct diagnosis had not been made during life. The patient died from peritonitis. In Dr. Crane's case I did not understand exactly how much time elapsed after the diagnosis was made, before operative intervention was undertaken.

Dr. Crane. The next day.

Dr. LeWald. As Dr. Crane has explained, the findings would mean there was already an infection which resulted in a fatal termination, just as we see sometimes in common duct obstruction, where there is a suppurative condition of the liver, although, as Dr. Crane has said, that is relatively rare. The case, I think, is of unusual interest and Dr. Crane certainly reported it in a very interesting manner.

Dr. Crane (closing). I have nothing more to say except to add that in looking up the literature we didn't confine ourselves to gallstone obstruction of the duodenum, or perforation of the gall-bladder into the duodenum. It is a scientific author's duty to state what the paper is about in the title so in the literature anybody who is looking for information can find it.

THE VALUE OF ROENTGENOGRAPHY IN THE DIAGNOSIS OF CONGENITAL SYPHILIS*

INFANTS CONSIDERED

By EDWARD C. VOGT, M.D.

BOSTON, MASS.

THE value of any diagnostic procedure is dependent primarily on its accuracy. The chief purpose of this study was therefore to ascertain as nearly as possible how much we can depend upon the roentgenologic findings for the recognition of congenital syphilis in infants. Although it is generally conceded that the examination of the skeletal system is an important adjunct to diagnosis, the actual incidence of demonstrable bone lesions is probably not well realized.

The material here reviewed consisted of 109 infants under two years of age with what were considered proved diagnoses, and with complete clinical and roentgenologic records available. No cases were included that had antiluetic therapy before the first films were taken, for as will be noted later, luetic bone lesions heal rapidly with treatment.

The appearance of the specific changes will be considered only briefly in this paper, for that subject has been thorouthly presented by several competent authorities and for one of the most recent and complete résumés, reference may be made to the work of Pendergrass and Bromer.[3]

Since the majority of infants in this group were under one year of age (104 of the 109), they will be considered separately and dealt with first.

TABLE I

AGES BY MONTHS OF THOSE UNDER 1 YEAR

0–1	4
1–2	19
2–3	29
3–4	18
4–5	7
5–6	6
6–12	21
	104

As can be seen from the above table the majority of these infants were brought to the hospital in the early months of life. Sixty-three per cent were between one and four months of age.

The most common chief complaints, in order of frequency were: failure to gain or loss of weight; rash or skin lesions; snuffles or cold in the head; paralysis or failure to use one or more of the extremities (pseudo-paralysis). Less common were convulsions, diarrhea, vomiting, or localized tenderness.

The family history of course is very important in the diagnosis of congenital syphilis, but in many cases it is so unreliable that it will not be considered in detail here.

On physical examination snuffles, skin lesions, enlarged liver and spleen, and generalized adenopathy were the usual though not constant findings. Pseudo-paralysis was present in 22, hydrocephalus in 2 and dactylitis recognized clinically in only 4.

SEROLOGICAL REPORTS

Blood Wassermann reactions were recorded in 91 and found positive in 83, or 91.2 per cent. Eight were negative or doubtful. Of the cases listed as positive, 3 were reported negative on first examination, but subsequent blood test revealed them positive. Of the 13 remaining cases, Wassermann results were not recorded on the charts. Some of these had Kahn or Hinton tests instead, but in a few cases the Wassermann reports were evidently lost.

Spinal fluid Wassermann tests were done on 38 and only 7, or 16 per cent, were positive.

ROENTGENOLOGICAL PROCEDURE

Probably in no diagnostic procedure is technical precision more important. Films

* From the Medical and Roentgenological Departments of the Infant's and Children's Hospitals, Boston.

showing any motion or improper exposure should not be accepted. By using high milliamperage good detail can be obtained at 1/10 of a second without intensifying screens, and thus the necessity of retakes reduced to a minimum. An accurate timer is essential for duplication of results. For routine examinations, one view of each arm and hand (anteroposterior) and two views of the lower extremities (anteroposterior and lateral) seem sufficient. Films of the skull are sometimes indicated, but as will be shown later, the information sought is usually obtained from the long bones of the extremities.

CHARACTER OF LESIONS

Stated briefly, the signs readily recognized and of chief diagnostic importance are: (*a*) bone production as subperiosteal thickening; (*b*) bone destruction or osteomyelitis, and (*c*) disturbance of growth.

Subperiosteal thickening was the most frequent finding in this group, being present in 78 per cent of the cases. Periostitis is usually suggestive of lues but to be of much diagnostic value it should be bilateral and involve multiple bones. It is often accompanied by the signs (*b*) and (*c*). It must be differentiated from periostitis due to any other infectious process particularly tuberculosis and from the apparent subperiosteal thickening often seen in rickets (pseudoperiostitis).

Dactylitis, which is really a periostitis of the bones of the fingers, was noted in 16 per cent. In one case it was the only bone lesion recognized.

Osteomyelitis, evidenced by bone absorption and usually accompanied by new bone formation, was shown in 63 per cent. It most frequently occurs at or near the ends of the long bones, and may involve the epiphyses, but since cartilage is not opaque to the roentgen ray we cannot say from the films alone just when this does take place. There-

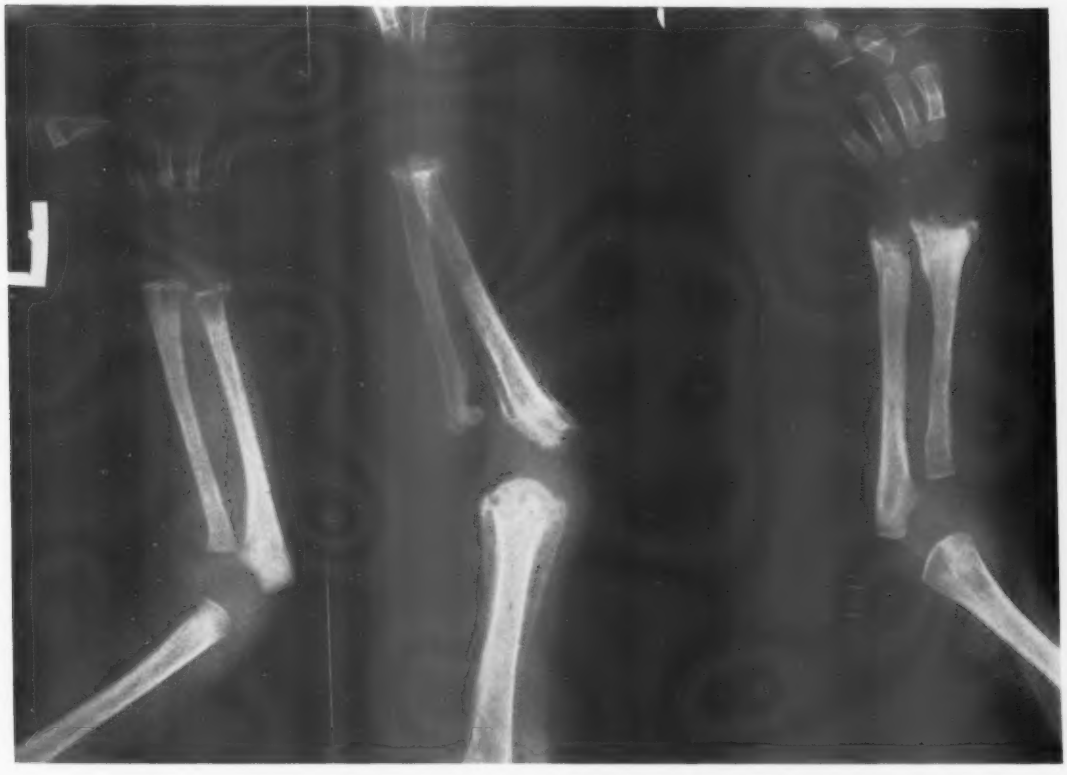

Fig. 1. Typical cases of luetic periostitis and osteomyelitis.

Fig. 2. Semilunar defects at the upper ends of the tibiae, pathognomonic of congenital syphilis.

fore the word osteochondritis is purposely omitted in this paper (see Fig. 1).

A special type of osteomyelitis, particularly as regards its location, is often seen as bilateral semilunar defects at the upper ends of the tibiae medially, adjacent to or just below the epiphyseal lines. This in my experience is pathognomonic of lues and was present in 45 per cent of this series (see Fig. 2).

Growth disturbance with or without other lesions can be demonstrated in a certain number. There may be only a dense narrow line at the ends of the diaphyses, but as such it is not diagnostic of syphilis, for this might be caused by developmental arrest resulting from any severe nutritional disturbance. In luetics, however, when the dense line is present, most cases will also show a parallel zone of diminished density just proximal, which is very suggestive. When the metaphyseal margins are serrated the findings are very characteristic (see Fig. 3).

Films of the skull were taken on 27 of the 104 cases. Seven of these showed either ir-

Fig. 3. Disturbances of growth at the ends of the bones of the forearms as shown by increased density and serrated margins.

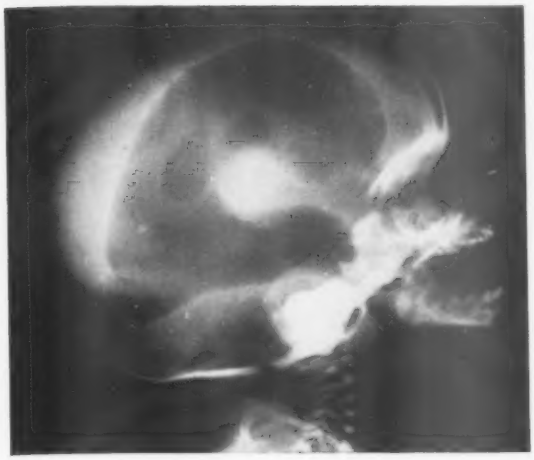

Fig. 4. Ventriculo-encephalogram of a five weeks old hydrocephalic luetic infant.

regular destruction or slight thickening of the cranial vault which was evidently of luetic origin. A common location for skull erosion is along the lambdoid and posterior portion of the sagittal sutures, with the result that a wide gap occurs in which there are multiple small bony spicules. Two cases showed separation of all the sutures which as far as the films were concerned could not be differentiated from any nonspecific hydrocephalus. All these cases under one year of age that showed skull involvment also showed diagnostic evidence of lues in the bones of the extremities.

Other roentgenological signs have been described and perhaps in a more detailed discussion of bone changes, certain additional criteria might be worth considering. However when reviewing doubtful material it is probably a less serious error to fail to recognize than to condemn unjustly the innocent parents of an unproved case. Sometimes even after the most careful study of the films it is not only impossible to make a definite diagnosis but there are what might be called degrees of uncertainty. Therefore it seemed logical to adopt the method used in reporting Wassermann reactions in order to impart as concise an opinion as possible. After a more or less detailed description of any lesions present, a final impression may be given to denote the interpretation placed on the findings.

MEANING OF REPORTS

1+ Bone changes which are either indefinite or which are likely to be due to causes other than syphilis. The diagnosis is doubtful.

2+ Changes that are suggestive of lues, but due to limited extent or lack of definite characteristics a diagnosis cannot be made without other evidence, either clinical or serological.

3+ Changes that are probably luetic in nature but which may occasionally be due to some other disease, e.g., tuberculosis.

4+ Characteristic bone lesions from which a definite diagnosis can be made.

Negative. When no bone changes are present which can be considered as being luetic.

Interpreted and tabulated according to the above method the results from the 104 cases under 1 year were as follows:

Table II

74	or 71.1	per cent 4+
15	or 14.4	per cent 3+
6	or 5.7	per cent 2+
3	or 2.8	per cent 1+(doubtful)
6	or 5.7	per cent negative.

Thus if we subtract the 9 cases that were either negative or doubtful, we have 95 varying between 2+ and 4+, or 91.3 per cent. In other words, bone lesions were actually present in that number, and a definite diagnosis of lues was made in 71.1 per cent.

Of these 8 cases all except one were under nine weeks of age, the exception being a boy of four months. His blood Wassermann was repeatedly negative but his Kahn test was positive. His father and mother were both luetic and the Wassermann test on a small brother was positive. He had been born one month before term and had typical skin lesions. The only abnormal bone findings were dense lines at the metaphyseal margins which was considered 1+.

Eighteen cases had repeated examinations at intervals following the institution of antiluetic treatment and all showed progressive healing. Improvement was noted in some as early as two weeks but the time

required for complete healing of course depended on the extent of bone involvement. In some of the most advanced cases this took several months.

There is very little to be said about the 5 infants who were between one and two years of age. The long bones were considered negative in all of them. Skull films were obtained on 3 and one of these showed irregular erosion and widening of the margins of the lambdoid and posterior portion of the sagittal sutures. All were Wassermann positive and had clinical evidence of lues.

Table III

AGE AND BRIEF SUMMARY OF THE 8 CASES WITH NEGATIVE BLOOD WASSERMANN TESTS, TO SHOW BASIS FOR DIAGNOSIS.

No.	Age	Evidence of Lues in Parents	Clinical Evidence of Lues	Other Evidence of Lues	Bone Changes
1	1 mo.	Father and mother luetic	Yes		4+
2	5 wk.	Father and mother luetic	Yes	Hinton test positive	4+
3	5 wk.	Father luetic; mother blood Wassermann negative	Dactylitis	Improved with treatment	2+
4	6 wk.	Illegitimate child; mother blood Wassermann negative	Yes	Necropsy showed lues	4+
5	2 mo.	Father, Wassermann positive; mother Wassermann doubtful	Yes		4+
6	2 mo.	Father and mother luetic	Yes	Necropsy showed lues	3+
7	9 wk.	Father and mother luetic	Yes	Necropsy showed lues	3+
8	4 mo.	Father and mother luetic	Yes	Kahn test positive	1+

DISCUSSION

In general, the clinical and serological findings of this group were in close agreement with those of other writers[1,2] and tend to bear out the conclusion that a negative blood Wassermann in a child over two months of age is very good evidence against lues. Data other than the roentgenological were included to serve as a check on the accuracy of diagnoses and also for comparison of the incidence of bone lesions.

It should be understood that the final diagnosis always rested with the clinician in charge of the treatments. Two cases, not included in this group, had bone changes, which were called 4+ by the writer, but because of negative blood Wassermann tests, and lack of clinical evidence, they were not given antiluetic therapy. One of these came to necropsy and on microscopic examination of the bones a diagnosis of luetic periostitis was made. It is impossible to give an accurate estimate of the number of times certain nonspecific bone lesions were considered suggestive. Sometimes a low grade osteomyelitis may produce local-

ized changes closely resembling specific disease, but on checking up with films of all the long bones, lues can usually be ruled out. It would seem that with a fairly accurate conception of the characteristic bone changes, there should be very few false positive reports.

In attempting an explanation of the apparent wide difference in the incidence of the disease and in the roentgenological findings in known cases over one year of age, reference might be made to mortality tables of congenital luetics.[4] If untreated, a large percentage die during the first year. Those that live probably either develop a resistance to the disease or have a mild type of infection.

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EDITORIALS

EXPERIMENTAL AND CLINICAL LITERATURE ON RADIOTHERAPY

IF WE should judge from the current literature in radiotherapy it might appear that the greater part of the research carried out has been done on the physical side to the neglect of the biological reactions incident to radiation. This feeling is rather widespread and recently the *Lancet* stated that "there is an uncomfortable amount of truth in the gibe that the whole of radiology in its radiotherapeutic aspect lacks scientific basis and rests largely on an empirical footing." While it must be admitted that there is a modicum of truth in this statement, in this respect radiotherapy is not unlike a number of drugs which are used in the treatment of diseases, whose use began empirically and only within recent years has a scientific basis for their curative effects been established. There is, however, an enormous amount of literature, both experimental and clinical, upon which a rational basis for radiotherapy rests. Unfortunately, this material is scattered through various scientific publications in many languages and is not available for ready reference.

Realizing the inaccessibility of this material and the wealth of information which it contains, Dr. Desjardins was prompted to collect it, analyze it and make it available. In this issue we have the first installment of the first of a series of articles which the Journal has the pleasure of publishing. This first series deals with the "Action of Roentgen Rays and Radium upon the Gastrointestinal Tract; Experimental Data and Clinical Radiotherapy." The material has been arranged in chronologic order to facilitate reference and enable the reader to follow the historical development of the subject. The experiments with roentgen rays have been grouped separately from those with radium. These two groups of experimental reports Dr. Desjardins has subjected to a critical analysis and this follows the experimental reports themselves. This analysis in turn is followed by the clinical considerations in which is taken up the therapeutic application of roentgen rays and radium to every disease in which the particular tissues or organs are affected. Finally all of the data, experimental and clinical, are correlated and summed up. The comprehensiveness of this study is evidenced by the complete bibliography which accompanies each subject.

This series of articles represents an enormous amount of work on the part of Dr. Desjardins. They will add greatly to a knowledge of the scientific basis for radiotherapy and will go far toward dispelling the prevalent idea that radiotherapy lacks a scientific background. They will also prove invaluable to those who wish to carry out further experimental work along these lines. We cannot, therefore, too highly commend these articles to the Journal's readers.

ARTERIOGRAPHY

FROM the early days of roentgenography opaque substances have been injected into the arterial system of animals and especially of cadavers to determine the configuration and position of the arteries and their branches, but it has only been within comparatively recent times since the introduction of nontoxic iodine substances that arterial injections of opaque substances have been made in the living.

Among the first to employ opaque substances in the arterial injection of the human was Egas Moniz[1,2] who attempted and successfully accomplished arterial encephalography by injecting sodium iodide into the internal carotid. Later the method was changed somewhat and the contrast medium was injected after preliminary ligation of the external carotid, into the carotis communis. By this method he was able to obtain satisfactory arterial encephalograms which were in some instances of considerable diagnostic aid in the localization of intracranial neoplasms. He employed the method in more than forty cases without serious accident.[3] In nine cases, six of which were operated upon, a correct preoperative diagnosis was made.

Following the original publication of Moniz, three Portugese investigators reported before the Surgical Society of Paris on the technique of abdominal aortographie. More recently these same investigators[4] have reported the results of their continued experimentation in this field and they not only have perfected the technique of their procedure but by employing some of the more recent less toxic iodine compounds, the method of injection has been somewhat modified. Their procedure is relatively simple. To obviate the pain which is associated with the injection they have employed a local anesthesia at the point selected for the injection. A needle 12 cm. in length and of 1.2 mm. caliber is introduced four fingers breadth to the left side of the spine under the twelfth rib paralleling it and directing the needle toward the aorta between the twelfth dorsal and first lumbar segments. Preliminary to the injection tourniquets are applied to the upper part of the thighs to aid in the concentration of the dye. When the needle has been introduced 10 or 11 cm. in the direction of the aorta, a novocaine solution is introduced as a local anesthetic. After waiting about five minutes the needle is pushed gently forward into the aorta. After being certain that the aorta has been punctured, as evidenced by the intermittent flow of blood corresponding to the rhythm of the pulse, the introduction of the opaque solution is made. Twenty grams of abrodil (the usual dose used in intravenous pyelography) is introduced under 2 kg. pressure at the rate of about 5 c.c. per second. The stereoscopic roentgenograms are made during the injection, a Potter-Bucky diaphragm being used to obtain sufficient detail. The resultant roentgenograms which are obtained by this method are, as shown in the illustrations in the original article, of splendid quality outlining the entire abdominal aorta with its various branches. Not only does this method permit the visualization of the abdominal aorta and its branches, including the renal and uterine branches, but at the same time one is able to obtain the outline of the excretory anatomy of the kidney. The method may be a means of throwing considerable light on some of the obscure physiological processes of the abdominal viscera and it will undoubtedly be of aid in the diagnosis of abdominal tumors.

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SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. John T. Murphy, 421 Michigan St., Toledo, Ohio.
Thirty-second annual meeting: Haddon Hall, Atlantic City, N. J., Sept. 22-25, 1931.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: New Orleans, La., 1932.

Section on Radiology, American Medical Association
Secretary, Dr. G. W. Grier, Jenkins Arcade, Pittsburgh, Pa.
Annual meeting: New Orleans, La., 1932.

Radiological Society of North America
Secretary, Dr. I. S. Trostler, 812 Marshall Field Annex, Chicago, Ill.
Seventeenth annual session: Hotel Jefferson, St. Louis, Mo., Nov. 30–Dec. 4, 1931.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. John F. Chapman, 209 Professional Bldg., Pasadena, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. W. S. Lawrence, Medical Arts Bldg., Memphis, Tenn.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N.Y.
Meets monthly on the first Tuesday from October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St.
Meets second Monday of each month except during the summer months, the place of meeting to be selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

Cleveland Radiological Society
Secretary, Dr. A. Srauss, 518 Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Illinois Radiological Society
Secretary, Dr. Fauntleroy Flinn, 220 South Webster St., Decatur, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.
Next meeting: Rochester, Minn., October, 1931

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. J. Bennett Edwards, Englewood Hospital, Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. Robert C. Hall, 258 Genesee St., Utica, N.Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next meeting, to be announced.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 p.m., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary-Treasurer, Dr. E. W. Spinzig, 316 Metropolitan Bldg.
Meets first week of each month. Time and place of meetings designated by president.

Texas Radiological Society
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. B. D. Harrington, University Hospital, Ann Arbor, Mich.
Meets every Wednesday evening from October to June, at 7:30 o'clock in the amphitheatre of the University Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Next meeting, to be announced.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale.
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annualy in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Nicolae Busila, 44 Elizabeta Blvd., Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, 105 Rutledge Ave., Charleston, S. C.

THE GRID DIAPHRAGM APPLIED TO THE STEREOGRAPHIC STUDY OF THE MASTOIDS

By HOLLIS E. POTTER, M.D.
CHICAGO, ILLINOIS

USING the same stand with overhead arcs as was described in the June issue, together with a grid apparatus of the same size and design, it was found that the mastoids could be studied with the same facility as the paranasal sinuses. For this purpose the grid apparatus was incorporated in a housing of radically different design. The pose chosen for the patient was one sitting with head slightly bowed and inclined 45° to one side. For the opposite mastoid the grid unit must be swivelled half way around and the head inclined 45° to the other side. By keeping the grid apparatus as narrow as the short side of an 8″ × 10″ cassette, the mastoid goes easily to the center line of the grid without interfering with the shoulder.

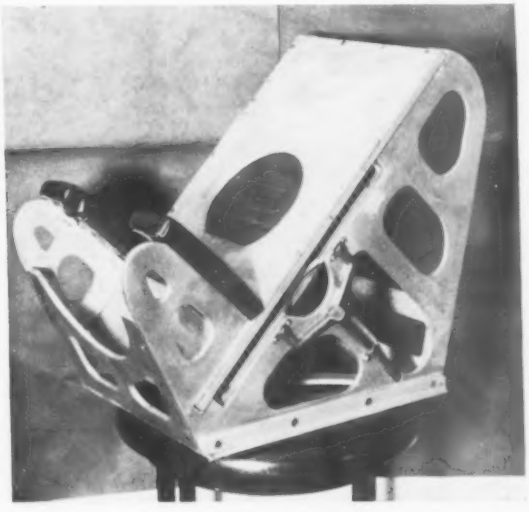

Fig. 1. The grid mastoid unit. Flanges at the base of the housing fit rotating sub-base to interchange with sinus unit.

The grid housing of cast aluminum is shown in Figures 1 and 2. The ear lies flat on the grid cover with chin and forehead resting against suitable pads. There is a free opening in front of the eyes and nose. The auricle is not turned back for with grid technique it interferes none when lying out flat. The mastoid thus centers over a 5 inch circular opening in protective lead and the circle is stationed over half of the 8″ × 10″ film. The opposite mastoid is recorded on the other half.

The grid apparatus is supported by hinges at the lower end so that for visual centering it can be dropped down and the position of the ear seen through the celluloid grid cover. In practical use this has proved unnecessary. The grid housing has a flanged base as in the sinus unit and fits upon the swivel sub-base in the same manner.

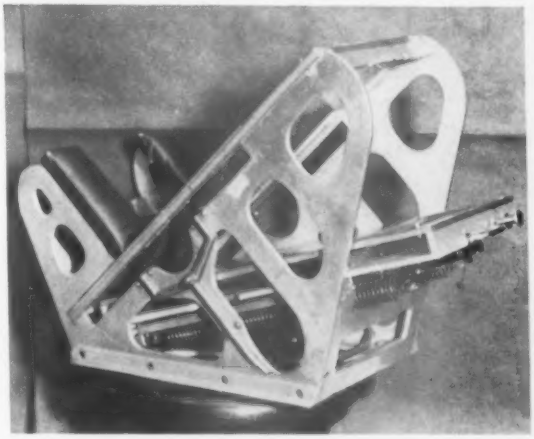

Fig. 2. The grid with its mechanism is flexibly mounted on hinges. Shown here in its lowered position.

* This is the fifth of a series of articles on diaphragming roentgen rays. The sixth article will appear in the August number of the Journal.—Ed

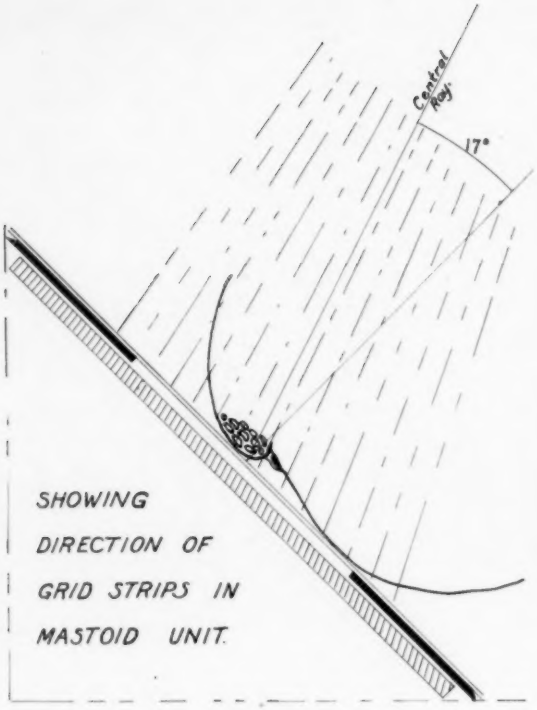

Fig. 3.

II. The *grid itself* is ¼ inch thick and built in a ratio of 1 to 4 as in the sinus diaphragm, but otherwise it is different. Because in mastoid roentgenography it is desirable that rays should not pass straight through the ear but at a considerable slant from above and behind, the grid was built so that all strips incline toward an operating point 20 inches away but 17° above the usual 90° angle used for grid diaphragms. This 17° angle is found to be satisfactory for all cases and the grid works out the same as at normal angle (see Fig. 3).

III. For a *stereoscopic set* of films of both mastoids two 8″ × 10″ films are used, on each of which a "right" and "left" is shown. Both rights are made before reversing the grid apparatus for the lefts. The stereo shift can be made on the tube carriage or by movement of the arcs. The latter is quite convenient since 7° on the arc is stereoscopic shift at 20 inches. This shift carries the rays in the same direction as the grid strips. With reference to the head it is a shift toward the vertex. Angles 23° and 30° are most often used (see Figs. 4 and 5).

Fig. 4. The mastoid falls naturally to center with the correct placement of the head. The auricle is not turned back.

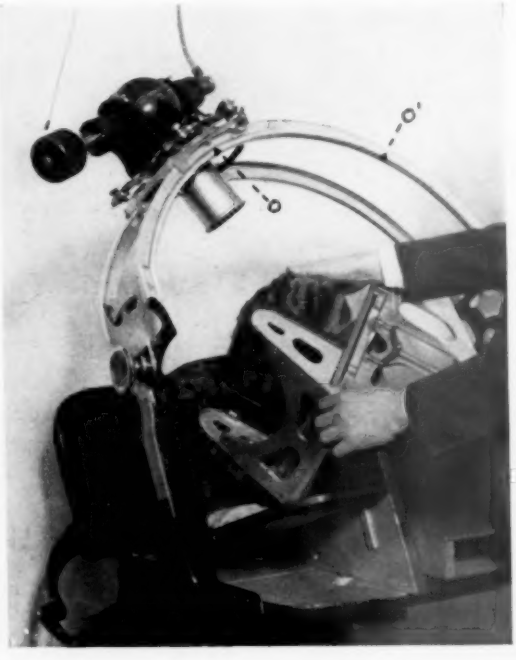

Fig. 5. Points o and o′ on the arc are at 17° from normal to grid. The grid is constructed to operate at this angle only.

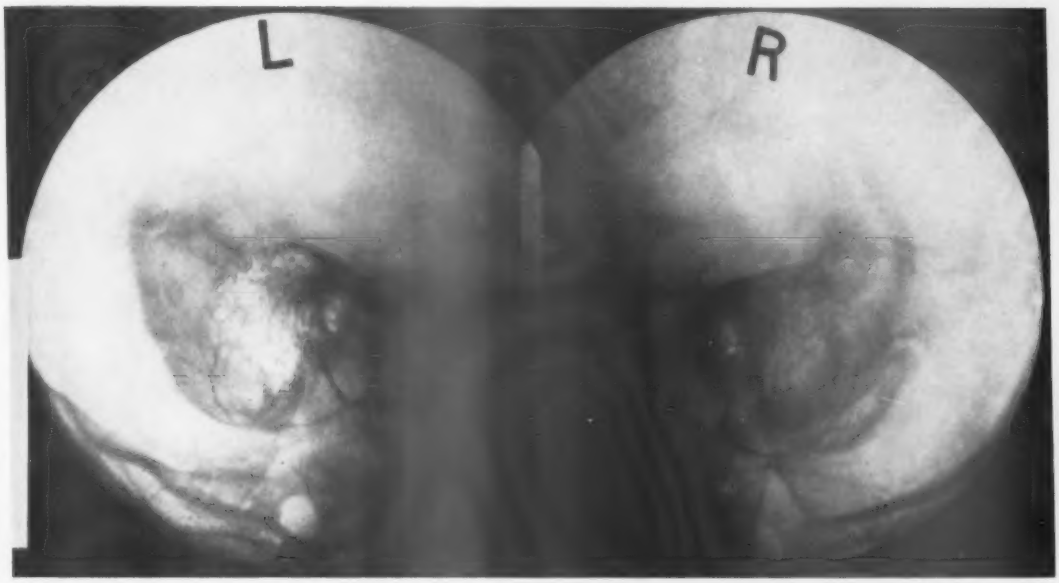

Fig. 6. Showing 5 inch circle for mastoid and regional structures. Right acute mastoiditis.

With this vertical shift the stero films must be viewed as if the patient were lying down. They can only be made with horizontal shift in case grid lines are avoided by modifying intensity of exposure as described in paper three of this series, if grid strips are placed at equal intervals.

IV. *New and various* angles of exposure may be found valuable and are capable of being repeated by keeping records of the degree readings on the arcs. After reading "Otologische Röntgendiagnostik" by E. G. Mayer, one should scarcely lay claim to new angles for mastoid roentgenography, but for a study of the tip cells one modified angle may be here recorded (see Fig. 8).

Fig. 7. Showing detail and contrast in intimate mastoid structures. Left mastoid necrosis.

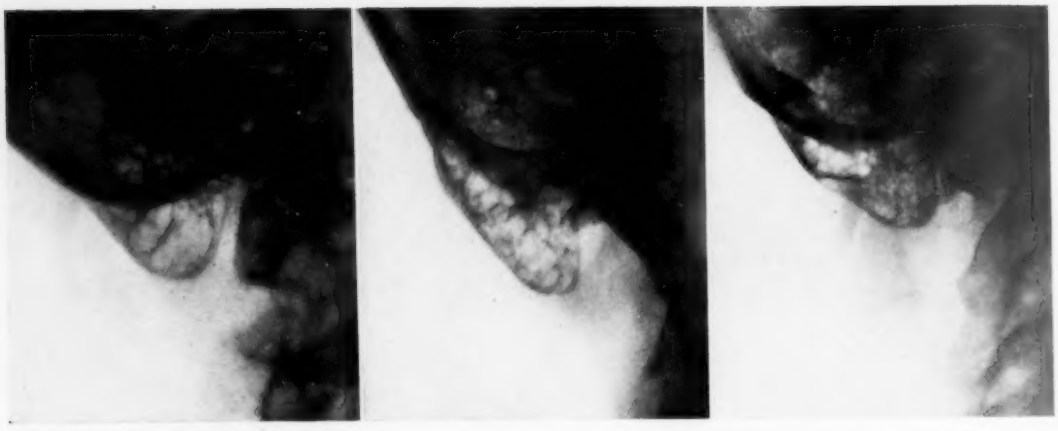

Fig. 8. An easy way to get tip cells clear of overlapping osseous structures.

Here the arc is simply lowered back till the rays pass through the tissues of the neck back of the vertebral column and through the mastoid cells. The main body of the mastoid is somewhat foreshortened on the film but the tip cells are rendered exceedingly visible because no bony tissues are superimposed and the mastoid lies near the film. The angle between the grid cover and rays is about 45°.

Other problems in special technique may be worked out with both the sinus and the mastoid units. The size and shape of the optic foramen viewed through the outer portion of orbit; the appearance of the ethmoid cells when thrown into the orbit; the anatomy of the temporomandibular region; the intimate structure of the lower jaw at several angles—these are a few of the problems which yield nicely to the facilities for angulation and grid clean up embodied in the apparatus. For general head roentgenography requiring a larger scope a third diaphragm apparatus taking a 10″ × 12″ cassette will be shown in the next paper, chiefly devoted to a description of a table accessory for the roentgenography of the stomach and duodenum.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Deep X-Ray Therapy in Malignant Disease. A report of an investigation carried out from 1924–1929 under the direction of the St. Bartholomew's Hospital Cancer Research Committee. By Walter M. Levitt, M.B., D.M.R.E., Medical Officer in Charge of the Radiotherapeutic Research Department. With an introduction by Sir Thomas Horder, Bart., K.C.V.O., M.D., F.R.C.P., Chairman of the Cancer Research Committee. Cloth. Price, 10s. 6d. Pp. 128, with 10 illustrations and 31 tables. London: John Murray, 1930.

This modest little volume from St. Bartholomew's Hospital in London with its unbiased discussion of technique and conscientious account of clinical results obtained under what must have been rather discouraging circumstances, since only the most hopeless cases reached the deep therapy department, does much to stimulate interest in the efficacy of short wave-length roentgen rays. In accordance with a plan elaborated by the Cancer Research Committee only those cases that were unsuitable for radium treatment or appeared to need more radiation than could be safely administered with radium were admitted for roentgen therapy.

Although the department is a small one, an attempt was made to carry out a careful study of the effect of changing some of the many variables which determine the roentgen dose. The results obtained with "excessive" filtration which is becoming popular in many parts of Europe, are contrasted with those obtained with the older techniques. With voltages in the neighborhood of 200,000, a marked preference is shown for a filter of 1.5 mm. of copper, although it is admitted that a "practical homogeneity of radiation" can be obtained with much thinner filters. It is, of course, necessary to increase the time of exposure but this objection is taken care of by utilizing what is known as the "intensive split dose method." The total dose is divided up into many fractions which are administered at regular intervals. Experimental and clinical investigations make it appear that the most efficient plan consists of delivering one fraction to the body every twenty-four hours. The total dose must be increased to compensate for the loss between treatments. Although no details are given, the results indicate that data such as those illustrated by Pfahler's saturation curves are used in making the necessary calculations. The number of fractional doses given to a single patient varied from 6 to 30, but the average patient received 12. The theory is advanced that the number of fractions should be larger with the slow-growing than with the rapidly growing tumor. This plan produces much less reaction than the old intensive single dose method and the results obtained in malignancy of the upper air passages and the uterus are superior to those resulting from the intensive technique.

All of the cases treated are classified under seven headings as follows: breast group, uterus group, upper air passage group, rectum group, esophagus group, thyroid group and lead cases. The plan of arranging ports and the factors used in each group are given in detail. In irregular areas such as the front of the neck and the breast, wax molds and powder bags were used to build up the irradiated region so as to obtain a more uniform radiation distribution. Brief chapters are devoted to the ward care of the patients and the constitutional effects of the treatment.

Some interesting observations as to general results are made. In almost every instance the patient showed a general improvement but it seems likely that this was due to two or three weeks of good hospital care as much as to the effects of the treatment. It was noted that outpatients did not progress as well as inmates of the hospital. Alcoholics and cases suffering from sepsis were difficult to handle and yielded poor results. Ulceration in primary tumors often healed, at least temporarily, but ulceration in metastatic glands reponded very poorly. Pain was relieved in some cases but not in others. Cervix cases almost always obtained some relief, whereas pain in the neck from enlarged cervical nodes and in the back and shoulder from carcinoma of the breast were rarely relieved. Hemorrhage and discharge were favorably influenced with great regularity.

The detailed results in each group are given

in tables. None of the groups were very large. There were 170 tumors of the upper air passages, 60 uterine, 50 breast, 26 rectal, 11 esophagus and 2 thyroid cases. In the breast group it was observed that the best results were obtained with a filter of 0.5 mm. of copper. Two cases are free of disease for three years and four others for lesser periods. None have remained well for five years. In the uterus group one patient with carcinoma of the fundus has remained free of the disease for four years and one for three years. No case of cancer of the cervix treated with roentgen rays alone has become entirely free of the disease. A small group treated with both radium and roentgen radiation showed somewhat better results. No definite conclusions were reached as to which should be given first. Two of the upper air passage cases are alive and free of signs of disease for four years, and twenty-four have been free of all signs of malignancy for lesser periods. The tumors treated include carcinoma, sarcoma, endothelioma, lymphoma and myeloma. The rectal cases did very poorly. None showed a disappearance of the disease and none lived more than one year. None of the esophagus patients were cured although one has lived more than a year and one showed a temporary disappearance of the tumor. Two thyroid patients were greatly improved but not cured by roentgen therapy.

In his conclusions, the author is puzzled by the fact that patients with the same type of carcinoma often respond differently to treatment. It seems possible that this difference could have been explained by grading the tumors on a histological basis. Very few histological data are given in the tables.

This book contains an honest account of what may be done for advanced cancer with deep roentgen therapy and seems to establish the value of heavy filtration and an intensive split dose technique. Being written in a scientific style, it is entirely free of fantastic claims and is therefore a very worthwhile contribution to radiological literature.

Charles L. Martin

Dental Roentgenology. By LeRoy M. Ennis, D.D.S., Assistant Professor of Roentgenology in the Thomas W. Evans Museum and Dental Institute School of Dentistry, University of Pennsylvania; Instructor in Dental Roentgenology in the Graduate School of Medicine, University of Pennsylvania, etc. Cloth. Price, $6.50. Pp. 288, with 582 illustrations. Philadelphia: Lea and Febiger, 1931.

This book has been written for the purpose of aiding the practising dental roentgenologist, as well as the student. All phases of the subject are presented concisely, yet thoroughly. The reproductions of the films and photographs are excellent, the films being reproduced in the negative, so that all structures appear as in the originals. This is an exceptionally fine feature because it aids the reader in more readily perceiving the structures described.

The first chapter contains all the necessary information concerning the roentgen tube, but at the same time is not so long as to become tiresome to a reader less interested in the physical aspects of the tube.

It is pleasing to note the mention of roentgen-ray dermatoses in the short second chapter. It seems to be the erroneous opinion of many persons that there is no danger during the operation of a dental machine, either to the patient or to the operator.

The third chapter, concerning the technique, is very clearly written, so that a student, with sufficient experience, may successfully employ the methods described. For the practising roentgenologist there are no doubt some helpful suggestions contained in this chapter. Contrary to the opinion of the author, some rentgenologists favor the use of the film holder. However, the resultant film is the important object, regardless of the method used to retain the film in the mouth during exposure.

The next chapter is an interesting description of methods which may be used in localizing abnormal conditions present in the jaws. It is of great importance that root fragments, unerupted teeth and foreign bodies, in particular, should be localized as thoroughly as possible because this procedure on the part of the roentgenologist often decreases the time necessary to complete the operation and conserves tissue in the region being operated upon.

The discussion of the chemical nature of the films and their processing, in the fifth chapter, presents concisely the necessity for rigid technique in the dark room.

It is admitted that a roentgen examination of the oral tissues does not constitute a complete examination upon which a final diagnosis

may be based. The author devotes the sixth chapter to emphasizing this fact.

Normal anatomical structures of both jaws are sometimes taken in a roentgen examination for abnormalities. In the seventh chapter there is given a comprehensive description of the most commonly mistaken structures.

The eighth chapter contains a detailed discussion of the pathological changes one may encounter in reading dental films. This and the preceding chapter are of the greatest importance to dental roentgenologists.

The last chapter contains suggestions which should be of great assistance in diagnosing root canal conditions and the information obtained should aid in making root canal treatment more successful. Again there should be mention of the detailed films and photographs which are so well reproduced. Especially in these last three chapters the illustrations are very valuable because they make it possible for the reader to see clearly what is being described verbally.

This book is one of the most thorough treatises upon this subject that has been published and will be a valuable addition to the library of anyone interested in dental roentgenology.

H. F. Doane

Books Received

Ergebnisse der medizinischen Strahlenforschung (Röntgendiagnostik, Röntgen-, Radium- und Lichttherapie). Band V. Herausgegeben von H. Holfelder, Frankfurt a. M., H. Holthusen, Hamburg, O. Jüngling, Stuttgart, H. Martius, Göttingen, and H. R. Schinz, Zürich. Paper, price M. 72.; bound, price M. 74.50. Pp. 675, with 396 figures in the text. Leipzig: Georg Thieme, 1931.

Die Röntgendiagnostik und -Therapie in der Zahnheilkunde (Radiologische Praktika. Band XVI.) Von Prof. Dr. Otto Loos, Frankfurt a. M., and Dr. Gerhard Gabriel, Frankfurt a. M. Cloth. Price, M. 36.00. Pp. 64, with 22 text figures and 257 photographic plates. Leipzig: Georg Thieme, 1931.

Röntgendiagnostik der Gallenblase. (Radiologische Praktika, Band XVII.) Von Priv.-Doz. Dr. F. Eisler and Dr. G. Kopstein. Cloth. Price, M. 18.60. Pp. 153, with 151 illustrations. Leipzig: Georg Thieme, 1931.

Einführung in die Röntgentherapie chirurgischer Erkrankungen. (Radiologische Praktika, Band XVIII.) Von Privatdozent Dr. Josef Palugyay, Leiter der Röntgenstation an der II. Chirurgischen Universitätsklinik in Wien. Cloth. Price, M. 10.00. Pp. 103. Leipzig: Georg Thieme, 1931.

Röntgenuntersuchung und Strahlenbehandlung der Speiseröhre. Von Dr. Josef Palugyay, Privatdozent für medizinische Röntgenologie, Leiter der Röntgenstation der II. Chirurgischen Universitätsklinik in Wien. Paper, RM. 56.00; bound, RM. 59.60. Pp. 391, with 224 illustrations. Wien: Julius Springer, 1931.

Röntgendiagnostik der Lungentuberkulose und ihre Bedeutung im Rahmen der Gesamtuntersuchung. Von Dr. Friedrich Koester, Leitender Arzt der Heilstätte Johannesstift Brilon-Wald i. W. und der Tuberkulosefürsorge im Kreise Brilon i. W. Paper. Price, RM. 2.80. Pp. 39, with 20 illustrations. Stuttgart: Ferdinand Enke, 1931.

Comment sont traités les rhumatisants chroniques dans le Service Central de Physiothérapie de l'Hôtel-Dieu de Paris. Par les Drs. H. Dausset, Chef du Service Central de Physiothérapie, L.-H. Dejust, Chef-Adjoint du Service Central de Physiothérapie, A. Chenilleau, Chef-Adjoint du Service Central de Physiothérapie, and L. Brace-Gillot, Assistante-Adjointe du Service Central de Physiothérapie, Attachée à la Consultation des Rhumatisants. Paper. Price, 12 Francs. Pp. 55, with 4 illustrations. Paris: L'Expansion Scientifique Française, 1931.

Il sussidio radiologico: nel trattamento dei traumi cranio-cerebrali (esclusi quelli d'arma da fuoco). By Prof. Olindo Alberti, Docente nell'Instituto di Radiologia, Radiologo Primario degli Spedali Civili di Brescia, and Dott. Fermo Mascherpa, Radiologo dell'Instituto di Neurologia. Paper. Pp. 194, with 152 illustrations. Roma: A. Manuzio, 1931.

Practical X-ray Treatment. By Arthur W. Erskine, M.D. Coth. Price, $3.50. Pp. 116, with 28 illustrations. Saint Paul and Minneapolis. The Bruce Publishing Co., 1931.

Laboratory Studies, Vol. xi and Clinical Studies, Vol. vii. From the Memorial Hospital, Huntington Fund for Cancer Research, Douglas Research Laboratory, New York City, 1930.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

PFAHLER, GEORGE E.: The study of the base of the skull 116
VANCEA, P.: Contribution to the study of intraocular magnetic foreign bodies 117

Neck and Chest

RUBIN, ELI H.: The course of tuberculosis in the lungs 118
GOLDBERG, BENJAMIN, and GASUL, BENJAMIN M.: Epituberculosis 119
HILLEMAND, P., CHENE, P., and SOULES, F.: A case of pyopneumothorax secondary to hydatid cyst of the lung 120
HABLISTON, CHARLES C.: Hernia of the mediastinum 120
UHR, J. S.: Subacute miliary tuberculosis; fatal case in an infant, with roentgenologic evidence of healing 121
BELOT, J., and PEUTEUIL, G.: The rounded opacities of the thorax 121
PANCOAST, HENRY K.: Roentgenology of the thymus in infancy and differential diagnoses of enlarged thymus and its treatment 123
BRAMS, WILLIAM A., and STRAUSS, HERMAN A.: The effect of amyl nitrite on the size of the heart and the width of the aortic shadow as determined roentgenologically 123
HURXTHAL, LEWIS M., MENARD, O. J., and BOGAN, M. E.: The size of the heart in goiter; a teleroentgenographic study 123

Abdomen

FELDMAN, MAURICE: The early recognition of gastric ulcer and carcinoma as revealed by roentgen-ray studies 123
CAULFIELD, ERNEST: An early case of pyloric stenosis 124
LEDOUX-LEBARD, R., and GARCIA-CALDERON, J.: Researches on the roentgen examination of the mucosa 124
DRAGULESCU, I.: The mobile duodenum 124
JACOTOT, P., and LACHAPÈLE, A.: The visualization of the biliary vesicle by cholecystography 125

Genitourinary System

HIRSCH, I. SETH: Urography by uroselectan .. 125
TRUCHOT and FALCOZ: The modifications of the rhythm of evacuation of the pelvis in the pyelonephrites 126
GOLDSTEIN, ALBERT E., and ABESHOUSE, BENJAMIN S.: Postoperative urinary incontinence 126

Skeletal System

COMPERE, EDWARD L.: The effect of phosphorus in rickets. I. Roentgenologic changes in rickets following the administration of phosphorus 126
RIGLER, LEO G., UDE, WALTER H., and HANSON, M. B.: Paravertebral abscess; an early roentgen sign of tuberculous spondylitis 127
BUCHMAN, JOSEPH, and GITTLEMAN, ISAAC, F.: Inorganic blood chemistry in the osteochondritides 127
BIVINGS, LEE: Staphylococcus albus septicemia with osteomyelitis of the pubic bone 128
LÉRI, A., LAYANI, F., and WEILL, J.: Dyschondro-osteosis; new variety of dwarfism 128
JAUBERT DE BEAUJEU, A.: A case of Pellegrini-Stieda's disease 129
PÉTRIGNANI, ROGER: Roentgen study of Pellegrini-Stieda's disease 129
MICHELSON, GABRIELE: On the question of the so-called "Stieda fracture" 130
BARTLETT, EDWIN I.: Periosteal lipoma 130
MATHEY-CORNAT, M.: Roentgen study of certain types of osseous myelomas 131

Blood and Lymph System

SAITO, MAKOTO, KAMIKAWA, KAZUNIRO, and YANAGIZAWA, HIDEYOSKI: New method of roentgenography of the arteries and veins on the living; its clinical applications for diagnostic purposes 131

ROENTGEN AND RADIUM THERAPY

LACASSAGNE, A.: Results of radiotherapy in adeno-epitheliomas of the uterus 132
VINZENT, RENÉ, and MONOD, OCTAVE: Study of the microbic flora of epitheliomas of the uterine cervix; its importance in radiotherapy 132
REGAUD, CL.: Radiophysiologic and medical sections of the Institute of Radium of the University of Paris: guiding principles, organization, function 133
HUET, J.-A., and SOBEL, A.: Note on the roentgen irradiation of the hypophysothalamic region 133
DELHERM, L., and BEAU, HENRI: Radiotherapy of the sympathetic in certain cardiovascular affections 134
CHANTRIOT, PIERRE: A case of lichen planus cured by roentgen irradiation of the sympathetic 135

Mahar, and Falcoz: A case of infantile hirsutism treated by radiotherapy..... 135
Chantriot: Keratodermia and irradiation of the cutaneous sympathetic..... 136
Birkett, G. E.: The principles of and some results in the radium treatment of buccal carcinoma..... 136
Quick, Douglas: Radium and surgery in cancer of the tongue..... 136
Cade, Stanford: The radium treatment of cancer of the tongue..... 137
Raynal, Albert: Irradiation by the perineal route..... 137
Lacassagne, A.: Indications of radiotherapy of sarcomas..... 138
Milani, Eugenio: Roentgen treatment in diseases of the blood-forming organs..... 138
Juul, Jens: Significance of the time factor in radium irradiation..... 139

MISCELLANEOUS

Kantner: The roentgen examination in technology..... 140
Chantraine, H.: On the intensifying screen in lung exposures..... 141
Boldingh, W. Hondius: A method of testing developer..... 141
Maino, Mario: Roentgen examination as a means of diagnosing death..... 141
Turano, Luigi: Changes in the capillaries on roentgen irradiation..... 141
Ko Muro-Hide o: Micro-chemical and cytologic findings in tissues of plants irradiated by roentgen rays. I. On "deep-stained cytoplasmic cell groups" in the tissues of root endings of *Vicia faba*..... 142
Mutscheller, A. Average quantum energy. A method of measuring it and its relation to the biological action of roentgen rays.. 142
Zimmern, A., and Chavany, J. A.: The radiosensitivity of nervous tissues..... 143
Gricouroff, Georges: Histological study of the action of roentgen rays on the ovary during the period of ovogenesis..... 144

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Pfahler, George E. The study of the base of the skull. *Radiology*, Sept., 1930, *15*, 339–352.

The paper is confined to the general technique for the study of the base of the skull and the special information obtained from such a study.

For the study of any of the changes in the bony structure of the accessory sinuses, it is absolutely essential to have perfect roentgenograms, which show the finest detail. A fine focus tube, the smallest possible diaphragm that will include the sinuses and no more; absolute stillness of the patient and the tube will be important factors. A localizer, illustrated in the paper, will assist in absolute direction of the central ray in relation to the accessory sinuses, and will permit the use of the smallest diaphragm. It is helpful and almost essential to make stereoscopic films in the sagittal plane shift. In his studies of the accessory sinuses, it is Pfahler's routine to make three stereoscopic films anteriorly with the shift in the sagittal plane, and with the central ray in the two shifts coming to the same point with a target-film distance of 22 inches. He then makes a lateral film at a target-film distance of 37 inches (which permits a smaller diaphragm and gives better perspective values than does a film made at closer range), and then a film of the base of the skull. The three stereoscopic exposures and the lateral view are each made on one-half of an 8×10 inch film, and the base of the skull film is also an 8×10, making three 8×10 inch films. When the conditions demand it, he makes also oblique films of the maxillary sinuses, or oblique films of the sphenoid region, or special films of the frontal and maxillary sinuses according to Waters' technique. All of these special studies are essential in some cases and probably would be useful in all, but the five routine exposures described above will usually give the necessary information and do not involve an excess of work or undue exposure to the patient, or unnecessary expense. The author describes the special head rest and localizer which he uses in making the stereoscopic films.

For demonstration of the base of the skull Pfahler has attached a wooden shelf $\frac{7}{8}\times 15\frac{1}{2}\times 20$ inches, supported by a brace at one end of his roentgenographic table, at a point 7 inches below the level of the top, and standing upward 20° from the horizontal. Upon this is placed a flat 11×14 inch Potter-Bucky diaphragm, which brings the upper surface 4 inches below the level of the top, and, of course, at the same 20° angle with the horizontal or level of the top of the table. For the exposure the tube is placed so that the central ray will be at an 80° angle to the plane of and at the center of the Potter-Bucky diaphragm, over the center of an 8×10 inch film between double intensifying screens, and at a target-film distance of 30 inches. A pillow about 3 inches thick (when compressed) is placed at the end of the table and the patient's head is allowed to hang over the end of the table so as to bring the top of the head in contact with the flat Potter-Bucky diaphragm and with the base of the skull in a plane parallel with the film. The head is held in place by a ring pad placed over the chin, over which is stretched the compression band. For the exposure he uses approximately 1 minute, 10 ma., 70 to 80 kv., at 30-inch target-film distance, with the 2 mm. glass filter, using an oval cone $3\frac{1}{2}\times 2\frac{1}{2}$ inches, which just covers, and an 8×10 inch film at 30-inch distance. He uses the Potter-Bucky diaphragm. When desirable, the posterior part of the base of the skull can be further studied by having the patient lie prone and bend the head forward so as to bring the base of the skull parallel with the plane of the film. In this latter position the shadow of the cervical spine is avoided, which is always demonstrable in the occipital region in the first position.

The author believes there is no single view of the skull that will give as much important information as that of the base of the skull, but he thinks it should form only a part of a general examination of the skull and should be a routine part of the study of the nasal accessory sinuses.

The normal skull and sinuses will show anteriorly the alveolar process, the teeth and the mandible forming the anterior and lateral borders of the ethmoid, maxillary, and sphenoid

sinuses. The frontal sinuses are rarely shown, and, when shown, are nearly obliterated by over-exposure. From front to rear the ethmoid cells divided by the nasal septum are recognized, then the sphenoid sinuses, the basilar plate, the anterior arch of the atlas, the odontoid process of the axis, the foramen magnum, and the occiput. On each side from front to rear, in the same order, may be recognized the middle and the posterior fossae of the skull, separated by the petrous portions of the temporal bone and the mastoid processes. Normally, the lines and the cancellous structures are sharply defined; the bone is evenly and symmetrically dense. The air-containing cavities show a symmetrical transparency and a general appearance of health.

The roentgenologic signs of acute superficial sinusitis are a cloudiness of the affected cavity. The walls show a decreased thickening, and at the same time an indistinctness or haziness in the acute stage. This indistinctness in and about the wall or at the borders is variable in extent, but in the films made especially of the frontal region when these sinuses are involved it can be recognized at times for more than one centimeter beyond the sinuses. At a later stage, this border on the outside of the sinus becomes denser than the surrounding bone, owing to an increase in lime deposit—the defense reaction in bone—and indicates an osteitis or perisinusitis.

The changes incident to chronic ethmoid-sphenoid sinusitis consist of a cloudiness, with a vague shading off of the anatomic details, accompanied frequently by a thickening of the posterior and lateral wall of increased density, which indicates an osteitis in the surrounding bone. This areola of dense bone corresponds in every detail to the perisinusitis in the frontal region previously described. This condition is not shown, except in association with sinusitis affecting the ethmoid or sphenoid sinuses. Therefore Hirtz and Worms have named this condition "perisinusite profounde." This perisinustis commonly extends into the middle fossa of the skull, but it may extend into the petrous and mastoid portions of the temporal bones, and even into the posterior fossa. At times, this deep perisinusitis is general and involves the base of the skull; at other times it is confined to one side, but it always corresponds to the side in which there is a deep sinusitis. Therefore, it must beconcluded that it is an extension of the inflammation directly from the affected sinus. This extension of the inflammation from sinusitis may also be recognized in the anterior fossa by means of the oblique frontal-plate position (Waters' position) and at times in the lateral position. This demonstration of the extension of the inflammation to the bones forming the base of the skull would lead one to assume that the dura mater, which takes the place of the periosteum on the inside of the skull, also becomes affected, as is indicated by a case reported in the paper in which the patient died from meningitis.

Pfahler has found these studies of value in determining the cause of obscure neuralgias, headaches, and ocular disturbances. Other pathological conditions which should also be demonstrated by this study of the base of the skull because of the ability to compare both sides are (1) brain tumor, which may show a pressure erosion or invasion which by its destructive process decreases the density of the affected bone; if a brain tumor contains lime deposit, it will be demonstrable by comparison with the opposite side; (2) fractures of the base of the skull; (3) anomalous conditions and congenital defects, and (4) extension of malignant disease from the nose, throat, or accessory sinuses.—*J. D. Camp*

Vancea, P. Contributtuni la studiul corpilor straini magnetici intraoculari. (Contribution to the study of intraocular magnetic foreign bodies.) *Cluj. med.*, Nov., 1930, *11*, 552–560.

The author describes and discusses in detail the various methods for the localization of foreign bodies within the eye. The methods are divided into three groups: (1) localization by means of two roentgenograms in the classical anteroposterior and lateral positions; (2) localization by shifting of the tube, the region of the eye remaining fixed, and (3) localization by roentgenograms of the eyeball taken in different positions, the roentgen tube remaining fixed.

To the first group belong the methods of Stoekl, Fox, Holth, Wessely, and others, all these being rather inaccurate and giving only a rough estimate of the position of the foreign body. To the second group belongs the method of Sweet (which is endorsed by the author), and to the third group the methods of Holzknecht, Belot and Fraudet.

The author, in association with Bendescu, has carried out a number of experiments for the

differential diagnosis of intra- and extraocular foreign bodies by means of injection of Tenon's capsule with water, air and opaque substances, but the procedure was found to be of little practical value.

For foreign bodies of very small size, which in routine examination may escape detection, the procedure of Vogt consisting in the roentgenography with films directly on the eyeball in the temporonasal and craniocaudal direction is recommended.

The author also discusses the value of the giant electromagnet for diagnostic purposes. In this respect three symptoms are of cardinal importance: (*a*) pain; (*b*) the bulging of the eye, and (*c*) hemorrhage in the anterior chamber produced by the approaching of the electromagnet to the eyeball.

Forty-two cases of foreign bodies were observed and studied by the author during the past few years, 12 of which were localized in the anterior portion and 30 in the posterior portion of the bulb. In 21 of the cases the diagnosis and localization were made by means of roentgenograms; in 10 cases by means of the giant electromagnet, and in 11 cases by means of both. The extraction succeeded in 22 cases; failed in 4 cases, and in 16 cases enucleation or eventration was required from the beginning.

The conclusion is reached that the presence of magnetic foreign bodies within the eye represents an exceptionally grave condition, requiring immediate intervention. Only in case the attempt to remove the foreign body has been unsuccessful is delay indicated. In such instances if the foreign body is well tolerated an operation may be abstained from, otherwise enucleation is advisable.—*T. Leucutia.*

NECK AND CHEST

Rubin, Eli H. The course of tuberculosis in the lungs. *Am. Rev. Tuberc.*, Dec., 1930, *22*, 710–716.

Chronic pulmonary tuberculosis usually makes its initial appearance in the right lung. As the disease progresses to the left lung it shows an increasing incidence of involvement. In male patients, the disease is usually detected when it is located in the right lung, whereas in females it usually involves both lungs when it is discovered.

RIGHT- AND LEFT-SIDED PREDOMINANCE IN VARIOUS STAGES OF PULMONARY TUBERCULOSIS

Author	Sex	Stage 1		Stage 2		Stage 3		
		Rt.	Lt.	Rt.	Lt.	Rt.	Lt.	Total
Williams (1)	Both sexes	287	168	55	69	43	53	675
Strandgaard (2)	Males	348	78	231	154	139	179	1,129
	Females	319	59	154	98	101	182	913
		667	137	385	252	240	361	2,042
Tecon and Aimard (3)	Both sexes	374	142	580	472	163	269	2,000
Cavalcanti (4)	Both sexes	111	58	151	141	133	159	753
Total		1,439	505	1,171	934	579	842	5,470
Percentage Rt. & Lt.		74%	26%	56%	44%	41%	59%	

Pulmonary tuberculosis does not pursue an even course. The site of activity vacillates from lobe to lobe, lung to lung, etc. When tuberculosis spreads caudally after a period of quiescence the process is not as fulminating as when it spreads to the opposite lung. Secondary extensions are usually more acute than initial implantations, and occur more frequently in the left lung.

Several reasons are related as to the possible cause of relative benignity of lesions of the

INCIDENCE OF RIGHT-SIDED AND LEFT-SIDED ARTIFICIAL PNEUMOTHORACES

Source	Total	Rt.-sided pneumothorax	Per cent	Lt.-sided pneumothorax	Per cent
Brauns (12)	63	20	32	43	68
Bronfin (quoted by Sewall) (13)	57	24	42	33	58
Neumann and Wolf (14)	150	67	45	83	55
Dumarest and Brette (15)	256	90	35	166	65
Alvermann (16)	773	368	48	405	52
Morris (17)	197	92	47	105	53
Harms (18)	205	99	48	106	52
Miller (19)	50	16	32	34	68
Kendall and Alexander (20)	131	55	42	76	58
Cooper and Stallings (21)	418	186	44	232	56
Author	122	57	48	65	52
Total	2,422	1,074	44.3	1,348	55.7

right lung as compared with the left, and the greater frequency of pneumothorax on the left than on the right.

Tuberculous pneumothorax is more likely to occur in patients with acute pulmonary disease in whom protection by pleural adhesions is incomplete or lacking, and it occurs more frequently on the left side. Thoracoplastic operations are more frequently performed on the right side.

In conclusion, the author states that it seems more than a coincidence that in 55.7 per cent of the collected series of patients pneumothoraces were induced on the left side; that in 58.9 per cent pneumothoraces developed spontaneously in the left lung; that in 58.4 per cent thoracoplasties were performed to compress the left lung; and that in 59 per cent of the collected series of patients with advanced pulmonary tuberculosis the disease was found to be more extensive in the left lung. Although the differences are slight, they are sufficiently constant to suggest (1) that the left lung, more frequently than the right, is the seat of progressive disease that requires mechanical compression or is more liable to sustain spontaneous rupture as a result of the rapid evolution of the disease in that lung; (2) that the relative frequencies with which artificial and natural compressions occur in the two lungs are determined, primarily, by the nature of the disease in the right and left lungs at that stage of the disease in which such compressions are more likely to take place, and (3) that the tendency for chronic pulmonary tuberculosis to localize initially in the right lung and the characteristic mode of spread of the disease to the contralateral lung accounts for the greater frequency of artificial and tuberculous pneumothoraces in the left lung.—*E. P. Pendergrass.*

Goldberg, Benjamin, and Gasul, Benjamin M. Epituberculosis. *Am. J. M. Sc.*, Dec., 1930, *180*, 824–832.

Until recently pulmonary tuberculosis in children was regarded as extremely serious, and almost uniformly fatal. Eliasberg and Neuland were the first to demonstrate that this conception was erroneous. In 1920 these authors reported a series of tuberculous children with massive involvement, the roentgenologic appearance being a heavy, homogeneous density over the whole or greater part of the affected lobe. The density was usually sharply demarcated from the rest of the lung. The roentgen findings remained constant, usually for weeks or even months, without abrupt change. Following this there occurred a gradual diminution in the density of the affected lobe, and finally all roentgenographic evidence, with the exception of an enlarged hilum, disappeared. Physical findings disappeared and the only positive test remaining was the tuberculin reaction. The sputum examination was always negative for tubercle bacilli.

According to Eliasberg and Neuland the nature of these massive pulmonary involvements was a nonspecific infiltration on a specific tuberculous soil, and they called the condition epitubercular infiltration.

Although these authors were the first ones to bring out the characteristic clinical and roentgenographic appearances of this lung affection, the French medical literature called attention to this type of lung involvement as early as 1883 when Grancher presented a similar clinical case and called it spleno-pneumonia. Bourdel in 1886 in his book summarized the known facts regarding Grancher's spleno-pneumonia, and characterized it as a subacute bronchopneumonia similar microscopically to hypostatic congestion, but differing from it in that there was a sero-albuminous exudate in the alveoli. Hutinel in 1911 was the first one in France to point out the frequency which with spleno-pneumonia was associated with hilum tuberculosis. Sluka in 1912 described the triangular wedge-shaped infiltration around the hilar glands as being characteristic of a tuberculous involvement.

Since that time numerous authors have added various features to the original observation.

Goldberg and Gasul report 10 typical cases of epituberculous involvement in children which have been studied clinically and roentgenographically for a period of two years. All of the cases were tuberculous children who presented massive pulmonary involvement which either completely disappeared, or is still undergoing resolution.

The epituberculous infiltration is intimately associated with reactions of the tubercle bacillus or of its toxins. It is not clear whether the epituberculous area is a collateral inflammation or atelectasis from blockage by an enlarged hilar glandular process or whether it is a truly parenchymal tuberculous infiltration.

The authors include several roentgenograms illustrating the condition which they have presented.—*E. P. Pendergrass.*

Hillemand, P., Chêne, P., and Soules, F. Un cas de pyo-pneumothorax secondaire à un kyste hydatique du poumon. (A case of pyopneumothorax secondary to hydatid cyst of the lung.) *Presse méd.*, Nov. 29, 1930, *38*, 1626–1627.

The authors describe in detail a case of hydatid cyst of the left upper lobe which had perforated into the pleura, leading to a pyopneumothorax. The case was first observed in 1926 at which time the hydatid cyst was the size of a small orange. An operation was advised, but the patient refused to submit to it. The cyst slowly continued to enlarge in size until October 8, 1929, when it broke into the bronchus producing a fistula. October 16, 1929, the cyst broke into the pleura, leading to pyopneumothorax, with rapidly fatal outcome.

In analyzing the course of the cyst, the authors distinguish four periods: (1) benign evolution, lasting for several years; (2) suppuration of the cyst, with rapid deterioration in the general condition of the patient; (3) perforation into the bronchus; (4) perforation into the pleura.

Pyopneumothorax forms a rather rare complication of hydatid cyst.—*T. Leucutia.*

Habliston, Charles C. Hernia of the mediastinum. *Am. Rev. Tuberc.*, Dec., 1930, *22*, 702–709.

To the operator engaged in pneumothorax therapy who fails to constantly observe his patient under the roentgenoscope, much of great interest and utmost importance is hidden. Not only may the question of fluid, the type, the character of collapse secured, and the amount of pulmonary expansion in the collapsed lung during the phases of respiration, have a direct bearing on the amount and frequency of refills, but the displacement and the movement of the mediastinum during respiration may directly answer the symptoms of the patient and dictate the procedure of the operator.

Herniation of the mediastinum, while not frequently reported, is in all probability of greater occurrence than the literature on the subject would lead one to believe. The author reports the recent literature on this subject.

The displacement of the heart and mediastinum toward the contralateral side is a natural consequence of pneumothorax. In addition to this expected shift in structures, occasionally there is a protrusion of the pneumothorax cavity, past the median line and encroaching upon the pulmonary space of the contralateral side. Nitsch has shown that there are two "weak spots" in the mediastinum, the upper "weak spot" lying between the first and third ribs anteriorly, the site of the atrophied thymus gland. He found that a hernia in this area could be produced by creating a pneumothorax in the cadaver.

The other "weak spot" lies between the fifth and tenth dorsal spines posteriorly. Sauerbruch has pointed out the infrequency of hernias in

this locality, and states that when they do occur they are from right to left.

The infrequency of the occurrence of mediastinal hernia may be attributed to the mediastinal structures being rendered rigid by inflammatory disease, to pulmonary adhesions, and also to the fact that the diseased lung, collapsed, and in many instances lying in direct apposition to the mediastinum, adds dense tissues to the structures of the mediastinal "weak spots."

It is important in roentgen examinations to take films in expiration, otherwise herniation may not be demonstrable. The probability suggests itself that the infrequency with which this condition has been reported may be due to the fact that roentgen films of the chest are rather universally taken in full inspiration. The appearance of this condition is a signal to the pneumothorax operator to immediately reduce the hernia by aspiration of air from the pneumothorax cavity, and at the same time to lengthen the interval between them. Evidence in the literature is to the effect that once reduced the hernia has little tendency to recur, and that the therapeutic collapse can be cautiously continued. The importance of the discovery of the hernia is stressed by the fact that deaths have been reported from spontaneous rupture.

The pertinent facts in the literature regarding mediastinal hernias are as follows: (1) The occurrence is usually in the young, the age favoring a flexible mediastinum. (2) In the vast majority, the occurrence is through the upper and anterior mediastinal "weak spot." (3) Hernias have been seen usually following large refills of 500 to 1000 c.c. and in the presence of highly positive intrapleural pressures. (4) It may, however, occur in the presence of definitely negative intrapleural pressures. (5) Undue dyspnea is the most prominent symptom, which is relieved by aspiration of the pneumothorax cavity. (6) Large hernias may cause urgent symptoms and even death. (7) Rupture with the fatal production of bilateral pneumothorax may occur.—*E. P. Pendergrass.*

Uhr, J. S. Subacute miliary tuberculosis; fatal case in an infant, with roentgenologic evidence of healing. *Am. J. Dis. Child.*, Dec., 1930, *40*, 1269–1275.

Uhr reports a case of miliary tuberculosis in a child, aged two months, the roentgenograms showing extensive changes during the course of the disease in both lungs, the appearance being that of miliary tuberculosis. The lesions in the left lung apparently cleared up and healed. The roentgenograms of the ankles and lower legs showed marked swelling of the soft parts but no apparent bone involvement. From the history of contact with an actively tuberculous father and the subsequent roentgenologic examinations and positive von Pirquet test, Uhr thinks it is safe to assume that the disease began at or before the age of three months, when the child had an unexplained, sudden rise in temperature. From the mild course of the disease, as shown by the temperature curve, weight curve, and the absence of signs and symptoms, the duration of the disease (five and one-half months), and the clearing up of the process in the left lung, he thinks he was dealing with the subacute rather than the acute form of miliary tuberculosis. While miliary tuberculosis is almost always fatal, he reviews a number of cases, reported in the literature and substantiated by roentgenologic and clinical observations, which show that: (1) the disease is not always rapidly fatal, and (2) healing and recovery may occur.—*R. S. Bromer.*

Belot, J., and Peuteuil, G. Les opacités arrondies du thorax. (The rounded opacities of the thorax.) *J. de radiol. et d'électrol.*, Oct., 1930, *14*, 529–543.

The authors discuss in detail the diagnostic significance of the rounded shadows appearing within the chest. Generally they may be (A) intrapulmonary, (B) parietal, (C) mediastinal and (D) diaphragmatic. Within each group a differentiation must be made between (1) cysts, (2) malignant tumors, (3) benign tumors and (4) infectious processes.

The following diagnostic criteria are given: (A) intrapulmonary opacities; (1) Cysts; (*a*) hydatid cyst: as a rule solitary, homogeneous, spherical opacity of very slow evolution, occasionally producing reaction of the surrounding tissues; radioresistant; (*b*) dermoid cyst: originating within the mediastinum, always solitary, with sharp border, sometimes containing teeth and calcifications; (*c*) hematic cyst: solitary rounded shadow of mottled appearance, however with sharp borders and without further evolution; (*d*) cysticercosis: small multiple shadows, not very opaque, slowly enlarging in size.

(2) Malignant tumors: (*a*) primary and met-

astatic sarcoma—often multiple, spherical opacities with regular outline, of rapid growth without reaction of the parenchymatous tissues, radiosensitive; (*b*) primary and secondary cancer—mostly oval shadows, not very homogeneous, with irregular outline, surrounded by a zone of congestion and frequently associated with pleural reaction.

(3) Benign tumors: (*a*) lymphoid leucemia—rounded shadows, mostly parahilar, with regular contour and associated with mediastinal involvement; (*b*) lymphogranulomatosis—mediastinal masses, multiple pulmonary foci with or without infiltration of the pulmonary parenchyma; (*c*) neurinoma—solitary homogeneous shadow, with sharp regular outline, of mediastinal origin; (*d*) ganglioneuroma and pneumoliths—of varying form, very opaque.

(4) Infectious processes: (*a*) interlobar pleurisy, oval, the superior border slightly convex, reaction of the surrounding tissues; (*b*) pulmonary abscess—diffuse, grossly spherical shadow with unsharp margin and peripheral pneumonic reaction; (*c*) septic embolus—coin-shaped shadow, not very opaque, terminating rapidly either in absorption or suppuration; (*d*) infectious lobitis—nonhomogeneous, with irregular borders associated with cavities and parenchymatous changes; (*e*) pulmonary gangrene—oval focus, often containing a central cavity, producing marked reaction of the surrounding tissues, and showing rapid clinical evolution; (*f*) gumma—rounded shadow, not very opaque, often parahilar, with irregular border, not infrequently associated with pulmonary and bronchial sclerosis.

(B) Parietal; (1) Cysts: (*a*) pleural hydatid cyst—often semicircular, surrounded by a shell of pachypleuritis; (*b*) costal hydatid cyst—rather homogeneous, irregularly oval shadow, adherent to the thoracic wall and producing destruction of the ribs.

(2) Malignant tumors: (*a*) sarcoma of the ribs—hemispherical opacities, with sharp margins and moving with the ribs.

(3) Benign tumors: (*a*) pleural endothelioma; (*b*) pleural or costal fibroma and (*c*) fibrinous clot—all impossible to diagnose.

(4) Infectious processes: (*a*) encysted pleural effusion—homogeneous, fusiform shadow, occupying a tangential position to the thoracic wall; (*b*) cold abscess of the rib—same aspect as previous but with alteration of the rib;(*c*) pleural symphysis—complete opacity of the apex with curved inferior border.

(C) Mediastinum; (1) Vascular tumors—very opaque rounded shadows of varying form, with or without pulsation and frequently associated with mediastinitis.

(2) Benign tumors: (*a*) simple adenopathy, usually of moderate enlargement with polycyclic contours and juxtahilar calcified nodes; (*b*) Hodgkin's disease—dense polycyclic mass, often of very large size, involving the entire mediastinum, sometimes infiltrating the parenchyma or producing distant pulmonary foci, very radiosensitive; (*c*) fibroma—single, rounded mass with sharp border giving a cystic appearance; (*d*) substernal goiter—uni—or bilobated shadow, lying lateral or above the aorta, showing diminution of the opacity and elevation during cough and deglutition.

(3) Cysts: (*a*) dermoid cyst—single, opaque, often very voluminous with sharp border, sometimes containing teeth and calcifications; (*b*) hydatid cyst—rounded shadow with regular border, often associated with mediastinitis.

(4) Infectious processes: (*a*) mediastinal pleurisy—rather diffuse shadow often with sharp external borders.

(5) Malignant tumors: (*a*) thymic tumor—median shadow lying in the upper thorax, often bilobated, opaque, with sharp outline; (*b*) lymphadenoma—single tumor or enormous polycyclic masses of very rapid growth; (*c*) cancer of the esophagus—opaque, sometimes rounded shadow with irregular contours, not very homogeneous, chiefly in the posterior mediastinum.

(6)Vertebral abscess: (*a*) fusiform or pigeonnest shaped shadow, with alteration of the vertebral bodies.

(D) Diaphragmatic. (1) Neoplasm: (*a*) opacity of a cystic aspect but with rapid evolution; radiosensitive.

(2) Hydatid cyst—homogeneous shadow with sharp contour and slow growth, giving image of setting sun.

(3) Diaphragmatic encysted pleurisy—variable shape, occasionally rounded, not infrequently diffuse.

(4) Ectopic spleen—oval shadow lying against the left ribs, associated with hernia or absence of the diaphragm.

The article is illustrated with 48 beautiful and some very unusual roentgenograms showing all types of rounded intrathoracic shadow. —*T. Leucutia.*

Pancoast, Henry K. Roentgenology of the thymus in infancy and differential diagnoses of elarged thymus and its treatment. *Am. J. M. Sc.*, Dec., 1930, *180*, 745–767.

The thymic menace in infants is largely one of tracheostenosis, aided by relaxation of the soft tissues of the upper respiratory tract. Recurrent laryngeal paralysis is a most serious complication.

The diagnosis of enlarged thymus is made from an abnormal narrowing or bucking of the trachea at the thoracic inlet as it passes over the apex of the gland and is only shown in lateral views of the chest, and lateral deviation of the trachea is shown in the anteroposterior roentgenograms. The roentgen technique should be such that the examiner is able to exclude or diagnose high obstruction due to any cause. Sagittal and lateral views are made of the infant at the top of each phase of respiration. The therapy of enlarged thymus is discussed in detail.—*E. P. Pendergrass.*

Brams, William A., and Strauss, Herman A. The effect of amyl nitrite on the size of the heart and the width of the aortic shadow as determined roentgenologically. *Am. J. M. Sc.*, Nov., 1930, *180*, 618–620.

The authors make the following conclusions:

1. The size of the cardiac and the aortic shadow was studied roentgenologically in a series of 21 patients before and after administration of amyl nitrite.

2. The group studied included 6 normal persons and 15 showing clinical evidence of arteriosclerosis, with and without hypertension.

3. The transverse diameter of the heart shadow was reduced after amyl nitrite in 18 of the 21 persons studied. The presence or absense of arteriosclerosis of hypertension seemed to play a minor rôle in these changes in diameter.

4. The width of the aortic shadow was increased in 13 of the 21 patients after amyl nitrite. This result also seemed to be independent of the condition of the peripheral vessels or degree of blood pressure.

5. The changes in the cardiac diameter may perhaps be explained by the decreased content in the heart during diastole because of the rapid rate and displacement of blood into the dilated blood vessels and away from the heart.—*E. P. Pendergrass.*

Hurxthal, Lewis M., Menard, O. J., and Bogan, M. E. The size of the heart in goiter; a teleroentgenographic study. *Am. J. M. Sc.*, Dec., 1930, *180*, 772–781.

The authors have reported a rather interesting study which concerns cardiac enlargement as the result of hyperthyroidism. This question has long been unsettled, and one gains from the literature that cardiac enlargement from hypertrophy, or dilatation, or both, is a frequent finding in hyperthyroidism, and that it is due in some way to the disease in question. Statements have been made without sufficient statistical evidence to support this theory.

These authors studied 100 patients with hyperthyroidism and compared them with an equal number of patients with non-toxic goiter. The roentgenograms of the heart in these cases were taken at the usual 7-foot distance with the patient holding his breath in the mid-phase of respiration. The exposures were long so as to allow several pulsations of the heart. This prevented the error of obtaining the cardiac silhouette in either diastolic or systolic phase. From this, measurements were made. They concluded that no definite relationship could be found between the duration of the disease, weight loss, and the size of the heart.

The cardiac enlargement, as determined by the teleroentgenogram, showed a fairly direct relationship to age and coincident cardiovascular disease. The number of enlarged hearts of different degrees is practically the same in both the toxic and non-toxic goiter patient. If hyperthyroidism causes cardiac enlargement or hypertrophy and dilatation it is slight.—*E. P. Pendergrass.*

ABDOMEN

Feldman, Maurice. The early recognition of gastric ulcer and carcinoma as revealed by roentgen-ray studies. *Radiology*, Oct., 1930, *15*, 449–456.

The early signs of gastric disease as determined by radiological methods are presented, with a description of these findings. The importance of arriving at an early diagnosis without the presence of an organic filling defect is stressed. Feldman states that the fluoroscopic examination in the early stages of gastric disease may not reveal any abnormal changes, but that a series of films usually presents evidence of spasm or abnormal peristalsis. Frequent roentgen examinations are often necessitated, especially when the roentgen diagnosis and the clinical findings do not appear to be in accord.

The author believes (1) that a stereotyped, fixed, or straight line appearance of the curvatures of the stomach as revealed by roentgen examination occurs as the result of a thickening, induration, and infiltration of the tissues of this organ; (2) that diminished or absent peristalsis or a break in the peristaltic wave is probably the earliest roentgen sign of gastric disease; (3) that a small stomach, located high, presenting the fixed and stereotyped appearance, emptying rapidly, even though showing no filling defect, is frequently the result of a carcinoma at the cardia of the stomach; (4) that spasm is frequently the result of a gastric lesion, occurring in 16 per cent of his cases of ulceration; (5) that the presence of a filling defect is not always necessary in order to establish the roentgen diagnosis of a gastric lesion, and (6) that the proper interpretation and evaluation of the roentgen signs described in the paper is highly important in the early diagnosis of gastric disease.—*J. D. Camp.*

Caulfield, Ernest. An early case of pyloric stenosis. *Am. J. Dis. Child.*, Nov., 1930, *40*, 1069–1075.

Author's summary and comment: Patrick Blair M.D., F.R.S., gained a notable distinction as an anatomist and botanist among the physicians and scientists of the early eighteenth century.

In 1717, he reported an unusual case before the Royal Society, which is probably the earliest description of pyloric stenosis in an infant. One cannot expect to find a twentieth century description of the disease; his unfamiliarity with the picture may account for some of the unusual features. There were a thick peritoneum, a small stomach and an involvement of the duodenum. But the balance of the description is so strikingly typical that it admits of little doubt of the identity of the disease. Among the outstanding features that would be difficult to reconcile with any other diagnosis may be mentioned: the sudden onset at the age of one month, the persistent vomiting throughout the illness, the eagerness for food, the extreme emaciation, the obstruction to food entering the intestines and the cartilaginous pylorus. The condition in the lungs admits of various interpretations, one being a terminal bronchopneumonia with abscess formation.

The life of Patrick Blair needs to be rewritten. There is a mass of unpublished correspondence among the Sloane manuscripts in the British Museum awaiting a biographer. This observant naturalist, botanist, pharmacologist and physician deserves to be remembered.—*R. S. Bromer.*

Ledoux-Lebard, R., and Garcia-Calderon, J. Recherches sur l'examen radiologique des muqueuses. (Researches on the roentgen examination of the mucosa.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 397–403.

The authors discuss the various media used for the roentgen visualization of the folds of the stomach and duodenum such as barium mixture, colloidal thorium dioxide, known under the name of umbrathor, thorotrast and uroselectan. Following this they describe the normal and abnormal appearance of the gastroduodenal mucosa in lengthy detail.—*T. Leucutia.*

Dragulescu, I. Duodenul mobil. (The mobile duodenum.) *Cluj. med.*, Dec., 1930, *11*, 606–608.

The mobile duodenum represents one of the most interesting forms of duodenal abnormalities. The mobility may be total or partial.

1. In total mobility, there is non-fixation of the mesoduodenum, the duodenal arch being free in its entirety, from the pylorus to the duodenojejunal angle. This anatomic disposition of the duodenum is encountered frequently in animals but in man it is exceedingly rare, the author finding a ratio of 1:2000 in the examined cases. The condition is without clinical significance. It produces no symptomatology unless complications arise (volvulus, hernia through the hiatus of Winslow, etc.). Pathogenetically the total mobility of the duodenum may be due (*a*) to a lack of torsion of the entire primitive intestinal tract, and (*b*) to a partial lack of torsion localized to the duodenal portion only.

2. In partial mobility of the duodenum there is non-fixation of only the second (descending) portion of the duodenum while the other portions show a normal fixation. This may be (*a*) complete, when the entire second portion of the duodenum shows non-fixation and (*b*) incomplete, when the non-fixation is localized only to the superior segment of the second portion of the duodenum. The first often results in an infravaterian duodenal stenosis, while in the second the stenosis is always supravaterian. Clini-

cally both forms of partial mobility of the duodenum are characterized by two cardinal symptoms: pain, which usually starts in childhood, comes on four to six hours after meals and is relieved in horizontal decubitus; and icterus, which in the beginning is light, appears only temporarily following a painful attack but which later may become very pronounced, febrile and of a more or less permanent character.

Roentgenologically the complete form shows a reversed U appearance of the duodenum, while the incomplete form gives a more complicated picture, not infrequently leading to the superimposition of the three segments of the second portion of the duodenum.

The therapy in total mobility of the duodenum is chiefly medical, while in partial mobility, surgery (duodenojejunostomy, section of Treitz's muscle and fixation of the duodenum) is indicated.—*T. Leucutia.*

Jacotot, P., and Lachapèle, A. L'objectivation de la vésicule biliaire par la cholécystographie. (The visualization of the biliary vesicle by cholecystography.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 381–389.

The authors discuss the value of cholecystography according to the method of Graham and Cole, emphasizing especially the following points: (1) physiologic basis; (2) current techniques of use, their advantages and disadvantages; (3) procedure of roentgen exploration, and (4) results obtained.—*T. Leucutia.*

GENITOURINARY SYSTEM

Hirsch, I. Seth. Urography by uroselectan. *Radiology*, Oct., 1930, *15*, 480–486.

Uroselectan is a drug which is non-toxic, easily soluble in water, and is excreted by the kidney in a concentration high enough to give the necessary roentgenologic contrast. Neither in solution nor in its excreted form is the iodine present in an inorganic, ionized state. Because of this, in spite of the relatively large quantity of the calculated iodine element in uroselectan, it can be administered with impunity. The method is based on the excretion of the contrast substance by the kidneys. The more normal the kidneys, the greater the excretion, and the earlier, the more constant and complete is the delineation of the urinary tract. Since about 90 per cent or more of the iodine content can be recovered in the urine within from six to eight hours, in cases with normal kidney function, uroselectan is a test of renal function in addition to a urographic medium.

The method permits study of the urinary tract under normal conditions in the living. The lack of uniformity in the morphologic characteristics of the ureter is one of the striking features which this examination has disclosed. Intravenous urography shows for the first time the physiological functional variations and permits the study of tone and peristalsis of the ureter and pelvis of the kidney.

The conclusions regarding disturbed function are based on the time of visualization of the contrast substance and the degree of density of the shadow. The actual standard of density is arbitrary and depends on a comparison of the two sides and the general structural density as shown in the roentgenogram. Sharp and clear visualization may be expected only when the kidney function is normal. Depending on the degree of parenchymal damage, there is poor or delayed or no visualization whatever. If there is no outlining of the pelvis and calyces, it is either because there is no kidney or the function has been destroyed. Malformations in which function is maintained are clearly delineated. General lowering of the functional efficiency of the urinary system, as in severe cardiac failure, may be responsible for non-visualization; visualization may also be poor in cases of infection in the urinary tract.

Intravenous urography is indicated in cases in which anatomical and pathological obstacles exist for cystoscopy, ureteral catheterization, or instrumental pyelography; in cases in which there is ureteral obstruction and the pyelographic solution cannot be injected beyond the obstruction, and in cases in which instrumental pyelography is definitely contraindicated or not convenient. It should be used in those cases in which cystoscopy and ureteral catheterization are difficult or impossible, namely, in urethral strictures, severe bladder disease and severe bleeding, in cases in which the ureters cannot be catheterized and in which catheterization gives no definite information; in cases of ruptured kidney; in fistulae; in cases in which the ureters have been transplanted; in those cases in which instrumental pyelography should not be done—in acute and chronic disease of the adnexa, in tuberculosis, in cases of prostatic hypertrophy—and in infants and children.

The technique of intravenous urography is described.

Hirsch believes that intravenous urography will undoubtedly solve many urological problems without the aid of cystoscopy and ureteral catheterization, and will probably replace catheter pyelography as the method of choice. It will not replace the catheter for the determination of the source of blood and pus, nor for the segregation of the kidney urine. It may attain the status of a renal function test, but it will not do away with ureteral catheterization entirely. —*J. D. Camp.*

Truchot and Falcoz. Les modifications du rythme de l'évacuation du bassinet dans les pyélonéphrites. (The modifications of the rhythm of evacuation of the pelvis in the pyelonephrites.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 361–363.

The authors have studied the rhythm of evacuation of the kidney pelvis and found that the following factors are of special importance: (1) the variations of the capacity; (2) the disturbances of the mode, and (3) the modifications of the duration of the evacuation. If an opaque fluid with a viscosity similar to that of the urine is cautiously injected into a normal kidney pelvis, without producing a distention which might disturb the peristalsis, one sees first the appearance of movements mixing the opaque liquid, then the formation of a ureteral bulb and finally the passage of the opaque substance into the ureter with simultaneous disappearance of the bulb. The rhythm varies within narrow limits from one patient to another, each evacuation following the preceding within two to five seconds, and lasting for a period of three to seven minutes.

In pyelonephritis, the following changes are found in relation to the above factors: (1) the capacity of the pelvis is expressed by the quantity of the injected fluid. The variations of capacity are not always in direct relation to the degree of the pelvic infection. (2) The disturbances of the mode of evacuation are very characteristic. In infections the contractions are sluggish and the formation of the bulb is prolonged. The evacuation occurs in the form of drippings, that is, by the gravity of the opaque liquid rather than by the active peristaltic movements of the pelvis. In consequence, the ureter remains outlined during the interval of passages of the opaque liquid, in most instances the peristaltic movement of the ureters being absent. All this results in rigidity, sclerosis and motor inhibition of the kidney pelvis and ureters. The frequency of contractions and evacuations is diminished in proportion to the degree of infection, the contractions occurring at intervals of from five to twenty seconds or more. In the very severe infections the contractions may be entirely missing, the evacuation of the liquid occurring by reflux (phenomenon of snowflakes). (3) The modifications of the duration of the evacuation are also very important. In all forms of pyelonephritis there is delayed evacuation, lasting in the very severe cases as long as thirty to forty minutes. The degree of delay can be used advantageously in estimating the prognosis and the response to treatment: a pyelonephritis which empties without a very marked delay will, as a rule, heal by the usual therapeutic procedures (lavage of the pelvis, vaccination, etc.), assuming of course that the focus of infection (of colon bacilli) in the intestinal tract has been removed, while if the evacuation is markedly delayed the pyelonephritis will continue to progress in spite of all treatment and will eventually develop into a pyelonephrosis with complete retention. —*T. Leucutia.*

Goldstein, Albert E., and Abeshouse, Benjamin S. Postoperative urinary incontinence. *Arch. Surg.*, Nov., 1930, *21*, 729–785.

In an exhaustive study of the literature and a report of a series of 220 prostatectomies, the authors state that urinary incontinence following suprapubic or perineal prostatectomy occurs more frequently than one would suspect. They have utilized cystograms to demonstrate the defects of the bladder in the cases in which they have had incontinence. The opaque solution is readily seen in the urethra.—*E. P. Pendergrass.*

SKELETAL SYSTEM

Compere, Edward L. The effect of phosphorus in rickets. I. Roentgenologic changes in rickets following the administration of phosphorus. *Am. J. Dis. Child.*, Nov., 1930, *40*, 941–967.

Compere reviews very thoroughly the literature covering phosphorus administration in rickets. Stimulated by the clinical studies of Phemister and his associates which seemed to show that the administration of phosphorus would bring about a cure of the disease, he un-

dertook a study of the value of phosphorus either alone or in combination with some other agents in the healing of the rachitic process. After the appearance of Phemister's work it was pointed out that diet and the summer season were factors that could not be excluded in bringing about the cures. Hess and Weinstock reported the results of their rat-feeding experiment which showed that the feeding of phosphorus did not prevent experimental rickets. Compere selected the fall and winter months for his investigation, Hess and Unger, Williams and others, having shown rather conclusively that the incidence of rickets increases during the fall and winter, and that the peak of the curve is reached in February or March. Throughout the author's experiments, the attempt was made to keep the environment, the hygienic conditions and the diet of the patients the same as those that characterized the period during which the rickets developed.

Compere summarizes the result of his investigations as follows:

1. Phosphorus alone was not sufficient medication to bring about healing in severe cases of infantile rickets in which there had been no initial stimulation from ultraviolet light or from cod liver oil.

2. Cod liver oil administered alone to infants with severe rickets, in dosage of from 3 to 6 teaspoonsfuls daily, brought about healing in most of the cases, although in two of the cases rickets had developed in spite of daily doses of cod liver oil for periods of several months.

3. Phosphorus administered in cases in which cod liver oil had been given and in which its administration was continued and in which other conditions, such as diet and home hygiene, remained the same, brought about prompt healing of the rickets and increased calcification of the shafts of the bones.

4. When patients had received elementary phosphorus in the form of one-hundredth grain pills (two such pills each day) for several months without improvement in the roentgenographic appearance of the bones, the healing response to the addition of cod liver oil was slow and the cure of the rickets was sometimes delayed for several months, although in every case studied, healing eventually occurred.

5. The combination of cod liver oil and of phosphorus administered to patients with rickets who had not received previous antirachitic treatment, even though this therapy was begun in the late fall or winter months when the incidence of rickets is known to be high, brought about prompt healing with marked calcification and increased density of all the bones studied by means of the roentgen rays.

6. The combination of cod liver oil and phosphorus produced more prompt and more certain healing of rickets than did cod liver oil alone.—*R. S. Bromer.*

Rigler, Leo G., Ude, Walter H., and Hanson, M. B. Paravertebral abscess; an early roentgen sign of tuberculous spondylitis. *Radiology*, Oct., 1930, *15*, 471–479.

The authors state that paravertebral abscess occurs very commonly in tuberculosis of the thoracic vertebrae but is clinically unrecognized in many cases. Its roentgen diagnosis is important because it is almost pathognomonic of tuberculous spondylitis. It may be the earliest roentgen sign of tuberculous spondylitis appearing before there are any visible changes in the bodies of the vertebrae. Two cases of this type are reported. It may be present in characteristic form while the changes in the vertebral column are still minimal or not entirely diagnostic roentgenographically. Two cases of this type are reported. Paravertebral abscess may overlap the shadow of the heart in the ordinary chest roentgenogram, simulating a mediastinal process.—*J. D. Camp.*

Buchman, Joseph, and Gittleman, Isaac F. Inorganic blood chemistry in the osteochondritides. *Am. J. Dis. Child.*, Dec., 1930, *40*, 1250–1261.

The search for the etiology of the various forms of osteochondritis has led some authors to believe that rickets is a causative factor. Clinical and roentgenologic studies, however, have failed to substantiate this assumption. The authors have reviewed the literature and have found that the few desultory studies on the inorganic blood chemistry, based on a limited number of cases, have given conflicting results.

In view of these conflicting reports, inorganic blood studies were made in 43 cases. The material included instances of vertebral epiphysitis, osteochondritis of the vertebral body, Legg-Perthes' disease, Osgood-Schlatter's disease, Köhler's disease of the tarsal scaphoid and cases of displaced upper femoral epiphyses. Several of the patients had multiple lesions. The lesions varied from mild to severe forms and

from early to late stages. The age limits of the patients extended from three to nineteen years. Potassium, magnesium and sodium determinations were made in 8 of these patients, in addition to the determination of the calcium and phosphorus content of the serum.

Recent investigations have shown that administration of thyroid extract mobilizes the calcium salts from the bones and may eventually lead to a severe degree of osteoporosis, while the calcium and phosphorus level of the blood serum remains normal. Similarly, toxic doses of parathyroid hormone increase the calcium and sometimes the inorganic phosphate of the serum at the expense of the bone. Certain chemicals, such as acid-yielding salts, liberate bone salts. Osteitis fibrosa cystica, in which there are local areas of osteoporosis and cyst formation in the bones, is associated with hypertrophy of the parathyroid glands. In rickets there is a deficiency either of inorganic phosphate or calcium or of both in the blood serum, with an excess of osteoid and other characteristic morphologic changes in the bones. It is this deficiency in the blood serum that some believe characterizes the disease and is responsible for the failure of bone salt deposition.

Buchman and Gittleman conclude from their study: (1) There is no evidence of rickets in their series of cases of osteochondritides as shown by the inorganic blood studies. (2) The inorganic phosphorus, calcium, sodium, potassium and magnesium content of the serum in this series of cases is well within normal limits. —*R. S. Bromer.*

Bivings, Lee. Staphylococcus albus septicemia with osteomyelitis of the pubic bone. *Am. J. Dis. Child.*, Dec., 1930, *40*, 1262–1268.

Bivings reports a case of *Staphylococcus albus* septicemia with osteomyelitis of the pubic bone. Septicemias caused by *Staphylococcus albus* are comparatively uncommon. When such infections of the *albus* variety do occur they are usually accompanied by numerous complications in the form of metastatic abscesses, and frequently terminate fatally or at least in some permanent disability. Osteomyelitis of the pubic bone from any cause is rare. His case is of peculiar interest because the patient recovered from the septicemia without other complications than the osteomyelitis and survived without surgical intervention. The patient, a boy aged seven, is now well and without disability.

The infection in Bivings' case seemed to have entered the blood stream from a crushed furuncle of the knee. Since the pubic bone is so rarely attacked and since in this instance there was no other complication, he regards it as probable that the infection spread directly to the pubic bone from the infected lymph nodes in that area. Local swelling and pain, which shifted from one locality to another would strengthen such a hypothesis. The diagnosis was established by the clinical course and by repeated blood cultures. The osteomyelitis was not suspected, but was discovered by the roentgenogram, and was followed throughout its entire course. Four serial roentgenograms are reproduced showing the bone destruction and repair. There was no evidence of involvement of the kidney at any time. Transfusions were considered but were not deemed advisable. Metaphen was given and it is interesting to note that the white cell count continued to climb daily as it was given, and it began to fall daily after its administration was discontinued. At one time during the course of the disease the roentgenogram showed a fracture of the ramus of the pubis. Recovery occurred without surgical intervention or spontaneous drainage.—*R. S. Bromer.*

Léri, A., Layani, F., and Weill, J. La dyschondrosteose; variété nouvelle de nanisme. (Dyschondro-osteosis; new variety of dwarfism.) *Presse méd.*, Feb. 21, 1931, *39*, 262–264.

The authors recently reported two unusual cases of dwarfism before the medical society of Paris (*Bull. et mém. Soc. d. hôp. de Paris*, Dec. 20, 1929, 1491 and Feb. 14, 1930, 385).

The height of the two patients was 136 cm. and 135 cm. respectively, the dwarfism being due chiefly to micromelia (shortening of the limbs). As compared with the dimensions of the trunk, there was a shortening of 20 and 22 cm. of the lower and of 30 and 34 cm. of the upper extremities. The hands and feet maintained an entirely normal appearance.

The roentgen examination revealed a marked shortening of the upper and lower extremities, localized chiefly to the bones of the middle segments (forearms and legs). There was almost complete absence of the upper end of the radius and of the lower end of the ulna, with lateral bowing of the shaft of the radius and posterior bowing of the shaft of the ulna on both sides. The tibiae and fibulae, except for the marked

shortening mentioned above, did not present any abnormalities. The bones of the rest of the skeleton (trunk and cranium) maintained their normal appearance.

Thus, briefly, the characteristic changes consisted in a very marked shortening of the limbs, localized chiefly to the mezomelic segment with a somewhat lesser shortening of the rhizomelic and integrity of the acromelic segment. There were no somatic disorders, the mental development, the various organs, the glandular and especially the genital system, being those of an adult. The personal and family history revealed nothing of importance.

The differential diagnosis includes Ollier's dyschrondroplasia, achondroplasia, rachitic and heredosyphilitic dwarfism, familial pleonosteosis, Madelung's disease and certain exostoses and anomalies localized to either the radius or ulna (radius curvus of Bertolotti, short ulna of Lévi, Bertolotti, etc.). The essential points in the differentiation of these conditions are briefly discussed.

The authors state that the two cases published are the only ones found in the literature. Due to the fact that the process is limited to the limbs, certain other bones showing normal appearance, the opinion is expressed that the condition is most probably a developmental disorder of later intrauterine life resulting in early ossification of the cartilages affected. For this reason, the term of "dyschrondro-osteosis" is suggested.—*T. Leucutia.*

Jaubert de Beaujeu, A. Un cas de maladie de Pellegrini-Stieda. (A case of Pellegrini-Stieda's disease.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 374–377.

Several cases of Pellegrini-Stieda's disease have recently been published in the literature. The author reports an additional case in a worker who fell from a considerable height, injuring his right knee. A roentgenogram two months later revealed a crescent-shaped shadow of 1 to 2 mm. thickness and 1.5 cm. length along the tubercle of the adductor brevis. The condition no doubt represents a post-traumatic justa-condyloid ossification.—*T. Leucutia.*

Pétrignani, Roger. Étude radiologique de la maladie de Pellegrini-Stieda. (Roentgen study of Pellegrini-Stieda's disease.) *J. de radiol. et d'électrol.*, Oct., 1930, *14*, 544–550.

The condition was first described by Pellegrini in 1905. A short report was made in the same year by Köhler but it was not until 1907 following the monograph of Stieda that the disease became known as a distinct entity. The clinical course may be briefly summarized as follows: An adult, after a relatively slight trauma (direct contusion of the internal aspect of the knee-joint or a fall in valgus position of the knee with external rotation and flexion of more than 90°), suffers from pain at the site of the internal condyle of the femur, later resulting in limitation of flexion and extension of the knee. At the beginning nothing serious is suspected but a roentgenogram taken a few weeks later reveals a characteristic calcification of the inner aspect of the knee along the internal condyle. The lesion may heal spontaneously or may result in more serious changes leading to traumatic arthritis with a permanent incapacity of 5 to 20 per cent.

The author describes in detail the technique of examination which must be in the antero-posterior and lateral views (both knees being roentgenographed for comparison) as well as the anatomic appearance of the normal knee (the internal condyle being divided into three—upper, middle and lower—zones) and the appearance of the pathologic shadow. In connection with this latter it is mentioned that the calcification may appear either at the level of the tubercle of the third adductor muscle or at the femoro-condyloid junction or at any of the three zones of the internal condyle. Its direction is vertical or slightly oblique and its form is one of the following: crescent-shaped, fusiform, elongated, vermiform, triangular or the form of an island, archipelago, sequestrum, mushroom, small button, spicule, etc. The lesion may be associated with the following changes: similar calcification at the external aspect of the articulation of the knee, ossification of the ligamenta cruciata, concomitant osteophytic productions, fracture of the internal condyle, and skeletal deformities such as genu valgum or varum.

It is recommended that in all cases of injuries to the inner aspect of the knee roentgenograms be taken not only immediately following the accident but also several weeks later to see if the calcification characteristic of Pellegrini-Stieda's disease has developed. The appearance of the shadow of the calcification as a rule occurs within fifteen days to several weeks following the trauma.

The differential diagnosis includes fracture of

the internal epicondyle of the femur occurring in any of the three zones mentioned, paraosteoarthropathies and more rarely osseous anomalies such as supracondyloid process, exostosis, osteoma, enchondroma of the joint capsule, etc.

The treatment in case the lesion does not clear up spontaneously consists in the operative removal of the calcification, followed by prophylactic roentgen therapy. If possible several roentgen exposures should be administered also previous to the operation.

The article is illustrated with several roentgenograms showing the findings in 10 cases observed or quoted by the author.—*T. Leucutia.*

MICHELSON, GABRIELE. Zur Frage der sogenannten "Stieda'schen Fractur." (On the question of the so-called "Stieda fracture.") *Röntgenpraxis*, Oct. 1, 1930, *2*, 896–898.

When Stieda in 1907 for the first time reported on the typical injury at the lower end of the femur, there can be no doubt that the condition in his case was the result of a fracture. König, Köhler, and Pfister, in 1909, first suggested that the Stieda shadow might have another etiology. They thought that since the shadow appears in the form of a narrow sickle-shaped opacity at the internal condyle of the femur, separated by a distinct transparent zone, it might be the result of a parosteal bone new formation and therefore they proposed the term of "fractureless callus formation." Ewald, in 1912, advanced the theory that the condition is the end-result of periosteal proliferation secondary to tear of the ligaments and tendons.

Schüller and Weil, in 1923, took the definite view that Stieda's disease represents a metaplastic parosteal new bone formation, the process never appearing within less than three weeks following injury. A similar opinion was expressed by Meyer and Alban Köhler.

All authors localized the shadow to the tendons of the adductor muscles, but they could not agree whether it was the result of direct or indirect trauma. In Ewald's material, no trauma could be demonstrated in the majority of instances. In the cases of Schüller and Weil, reflectoric muscle contractions due to incoordinated movements were thought to be the basis of the lesion. Finally Meyer admitted the possibility of both direct and indirect trauma as the provoking factor.

During the past five months, the author has observed 4 cases of Stieda's disease. The cases are briefly described and illustrated with roentgenograms.

An analysis of these cases reveals that in none was there evidence of direct trauma; in one the pain and ossification appeared immediately following a sharp contraction of the muscles and in the other three, some time later. The shadow of the ossification was structureless, of less density than that of the bone proper and always separated by a clearly defined zone.

In conclusion, the author endorses the standpoint of Schüller and Weil, considering Stieda's disease as a calcification and ossification of the fibers of the tendons and muscles rather than a splinter fracture of the lower end of the femur. The condition is not necessarily localized to the tendons of the adductors but it may occur also in the injured connective tissue. In most instances it is the result of indirect trauma.—*T. Leucutia.*

BARTLETT, EDWIN I. Periosteal lipoma. *Arch. Surg.*, Dec., 1930, Part 1, *21*, 1015–1022.

Malignant tumors arising from the periosteum or from structures immediately adjacent to the periosteum and growing out away from the bone without erosion of the bone cortex or invasion of the medullary cavity have been described by Ewing and Codman. At present these tumors are included among the bone tumors in the classification adopted by the Sarcoma Committee of the American College of Surgeons under the heading of periosteal fibrosarcoma. Since the publication of the classification of the Bone Sarcoma Committee much discussion has arisen as to whether these tumors rightly belong with bone tumors, because they seem to have no tendency to involve the bone and because there is no proof that they arise from bone structures.

The author reports two cases which had been diagnosed lipoma, both occurring in white boys, six and seven years old respectively. He shows excellent illustrations of the roentgenograms, and the lesion seems to be soft tissue in origin. One of the lesions occurred in the arm, and the other in the leg. The roentgenographic appearance is of a soft tissue tumor with some mottling and striation of the soft tissues. The mottling and striation of the soft tissues give a trabeculation or fan-like area which close to the bone would have to be differentiated from a periosteal osteogenic sarcoma. In the second case there was a depression in the fibula that sug-

gested some pressure or erosion of the bone. At operation, however, the depression was not due to an atrophy or involvement of the cortex.

The author concludes that it would be very difficult to make a clinical diagnosis in these lesions. Malignancy was not considered because of the large size of the growth, the intact periosteum in the sharp limits of the tumor, and the normal condition of the overlying skin and soft parts. At operation the tumor capsule and periosteum merged together and no line of cleavage could be demonstrated.

The first case was not diagnosed prior to operation, but the second case was so typical of the first that there was no hesitancy in making a diagnosis. The pathological diagnosis was lipoma. The author feels that these tumors may represent a benign counterpart of the malignant growth which has been generally called periosteal fibrosarcoma.—*E. P. Pendergrass.*

Mathey-Cornat, M. Étude radiologique de quelques types de myélomes osseux. (Roentgen study of certain types of osseous myelomas.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 393–394.

The author very briefly describes the roentgen findings in a case of multiple myeloma of the bone in a man seventy-one years of age. The condition started eight years previously, its chief characteristics being the appearance of repeated pathologic fractures (the first in the femur, the second in the humerus and the third in the elbow) and later a very pronounced enlargement of the cervical lymph nodes on one side. Following roentgen therapy there was a very marked improvement, the tumor of the neck having entirely disappeared. The histologic report was that of myeloma of the plasmocytoma type. The hematologic picture showed a leucocytosis and a polynucleosis without tendency to transformation into leucemia.—*T. Leucutia.*

BLOOD AND LYMPH SYSTEM

Saito, Makoto, Kamikawa, Kazuniro, and Yanagizawa, Hideyoski. Nouvelle méthode de radiographie des artères et des veines sur le vivant, ses applications cliniques au diagnostic. (New method of roentgenography of the arteries and veins in the living, its clinical applications for diagnostic purposes.) *Presse méd.*, Dec. 17, 1930, *38*, 1725–1729.

Moniz recently reported a method for the injection of the cerebral artery with sodium bromide solution for purposes of roentgenography (see abstracts this Journal, July, 1929, *22*, 79 and 80). The authors in experimenting with this method found that the injection of sodium bromide into the blood vessels often produces rather irritative symptoms such as pain, homolateral epileptic crises and even partial paralysis of the respiratory system. For this reason they have discontinued the use of sodium bromide and proceeded to the preparation of a new opaque substance which would do away with the above inconveniences. A careful review of the literature revealed that several substances, such as mercury, bismuth suspension, tetraiodochlorphthalein, calcium lactate, calcium chloride and iodide, dominal X, lipiodol, etc., had already been tried by other investigators without success.

A short time ago Hattori of the University of Tokio succeeded in producing from milk sodium-acid protalbuminate which he used for the preparation of a cod liver oil emulsion. Yanagizawa by mixing this preparation with lipiodol, obtained an excellent opaque emulsion which proved extremely satisfactory for the injection of the blood vessels. The emulsion, which is called "shadow," has a whitish lactic appearance, is neutral, produces no hemolytic action and does not coagulate the blood. Its injection into the blood vessels does not lead to emboli or any irritative symptoms. It is well tolerated at the rate of 5 c.c. per kilogram body weight. More recently several new modifications of the emulsion were prepared, the most important of which are the "shadow P" (lipiodol 25 gm., sodium-acid protalbuminate 0.75 gm., lecithin 10 gm., 5 per cent glucose solution 75 c.c.); "shadow E" (lipiodol 25 gm., egg white 6.1 gm., lecithin 10 gm., 5 per cent glucose solution 75 c.c.), and "shadow H" (lipiodol 25 gm., honey 10 gm., lecithin 10 gm., 5 per cent glucose solution 55 c.c.). The emulsion chiefly used in the current practice was "shadow P."

For the injection of the cerebral arteries, the authors first followed the procedure of Moniz, but later due to certain unexpected complications (hemorrhage, thrombus, etc.) they changed it as follows: one clamp is applied to the common carotid and a second to the external carotid just above the bifurcation of the superior thyroid artery, then under traction the superior thyroid artery is injected near its entry into the external carotid. The emulsion in this manner passes

from the superior thyroid artery through the external carotid into the internal carotid and thus to the arteries of the brain. Occasionally a thrombosis at the site of the injection was observed, but this being in a branch artery, proved of no significance.

For the injection of the arteries of the extremities, it is likewise advisable to use branch arteries: the superior collateral ulnar for the upper and the great anastomotic artery for the lower extremity.

The injections must be carried out as rapidly as possible by using a rather large needle (0.75 to 1 mm. in diameter). The quantity of the emulsion amounts to 7 to 10 c.c. for the cerebral arteries and 10 to 20 c.c. for the arteries of the extremities. The roentgenograms are taken at the end of the injection.

The method can also be used for the injection of the veins (venography). Two tourniquets are applied for this purpose, one above and the other below the part of the vein to be injected, the needle being inserted subcutaneously.

The procedure was used in 100 instances, not one single accident having been observed. Occasionally there was a slight abnormal sensation along the blood vessels, but no pain. Experiments carried out with regard to the anaphylactic accidents of "shadow P and E" (both containing albumin) in case of a second injection revealed that no such accidents occurred if the injections were made twenty days apart.

The method has a practical value especially in the following cases: arteriography of the brain in the living, localization of brain tumors, abnormal course of the arteries in healed fractures, diagnosis of arterial thrombosis in gangrene, modification of the blood vessels following amputation of the extremities, roentgenography of varices, etc. In cerebral arteriography, the authors were able to take stereoroentgenograms, either by injecting a larger quantity of the emulsion at one time (with a 20 c.c. syringe) or by injecting two smaller quantities successively.

Lately the emulsion has been successfully used also in pyelography, ureterography, salpingography, arthrography and myelography, as well as for the roentgen demonstration of fistulae, lacrymal ducts, the cavities of empyema, ductus deferens, epididymis, etc.

Chemical analysis of the urine revealed that the elimination of iodine started shortly following the injection and lasted for a period of seven to eight days. Due to this protracted elimination, one must assume a certain generalized therapeutic effect such as observed in bromotherapy following the injection of bromipin emulsion.

The conclusion is reached that the new emulsion introduced by the authors is entirely harmless, leading to some excellent results in both arterio- and venography. Several unusual roentgenograms are included in order to prove this contention.—*T. Leucutia.*

ROENTGEN AND RADIUM THERAPY

Lacassagne, A. Résultats de la radiothérapie des adénoépithéliomas de l'utérus. (Results of radiotherapy in adeno-epitheliomas of the uterus.) *Arch. Inst. du Radium de l'Univ. de Paris*, 1930, *2*, 133–142.

Summary. Opinions are divided among radiotherapists with regard to the best method of treatment in cancer of the corpus uteri. This no doubt is due to the uncertain clinical diagnosis, to the difficulty of removing a biopsy and especially to the inaccuracy of the histological diagnosis. Prismatic cell epitheliomas arising from the mucosa of the body of the uterus or from the glands of the cervix constitute a distinct group, best designated as adeno-epitheliomas of the uterus.

The results obtained at the Radium Institute of Paris in 30 cases of adeno-epitheliomas of the uterus, treated from 1919 to 1927, were considerably inferior to those obtained in other histological varieties of uterine epitheliomas. It seems therefore that surgery is the method of choice in the treatment of these lesions.—*T. Leucutia.*

Vinzent, René, and Monod, Octave. Étude de la flore microbienne des épithéliomas du col utérin.—Son importance pour la radiothérapie. (Study of the microbic flora of epitheliomas of the uterine cervix; its importance in radiotherapy.) *Arch. Inst. du Radium de l'Univ. de Paris*, 1930, *2*, 143–156.

Summary. The infection complicating radiotherapy of epitheliomas of the cervix uteri is not caused by any particular microbe; all uterovaginal flora may become virulent during the course of irradiation. The hemolytic streptococcus is the microbic agent most frequently encountered. Active antistreptococcic immunization (injections of emulsions of microbes

killed by heat, or dressings saturated with vaccines according to the method of Besredka) does not give constant results. In spite of the recent publications of the success with mixed vaccines, the prophylactic and specific treatment of the infections complicating radiotherapy is still consider impracticable. *T. Leucutia.*

Regaud, Cl. Les sections radiophysiologique et médicale de l'Institut du Radium de l'Université de Paris: principes directeurs, organisation, fonctionnement. (Radiophysiologic and medical sections of the Institute of Radium of the University of Paris: guiding principles, organization, function.) *Arch. Inst. du Radium de l'Univ. de Paris*, 1930, *2*, 157–245.

Summary. The close cooperation of radiophysiology with radiotherapy is essential for the progress of the latter. Roentgen therapy and curie therapy should not be separated in scientific research and practical application.

The application of methods of radiotherapy, especially to malignant diseases, demands a perfect organization and equipment, by reason of the exceptional difficulty of the task undertaken and the responsibilities which it entails in this branch of medicine. The attempt at organization should be directed to the quality and power of the institution and not to their number. It is advisable that a typical institution, especially organized for the radiotherapy of malignant diseases, should also treat patients suffering from benign affections, in order to keep in the institution the control of the difficult diagnoses, and to keep the incurable cancerous patients in ignorance of the exact diagnosis of their diseases. For the same reason the word cancer should not be exposed to the eyes of cancerous patients. It is useful for a scientific institution to associate with treatment investigations relative to human and experimental pathology of cancerous diseases.

Radiotherapy should not be the method used exclusively in the institution even if the object of this institution is to perfect and to teach techniques of radiotherapy. It is easier and preferable to add surgery to a typical institution for radiotherapy than to add radium and roentgen rays necessary for the cure of cancer to surgical clinics. The necessity of having in association men competent for different departments and sufficient equipment makes obligatory the creation of complete and powerful institutions and the limitation of their number. In no branch of medicine are the division and coördination of the work which govern teamwork, more indispensable than in the study and treatment of cancer.

All sorts of reasons concur to make distinct the two principal branches of medical radiotherapy: roentgen diagnosis and radiotherapy.

The special institutions are above all indispensable for the progress and teaching of radiotherapy. They have a double didactic task: general post-graduate teaching for general practitioners (early diagnosis, therapeutic indications, results obtained notably as far as cancers are concerned) and teaching of specialist (oral and practical teaching, clinical assistantships).

Roentgen rays and radioactive sources are not panaceas for cancerous diseases. The different varieties and localizations of cancer have given extremely unequal results from these methods of treatment. Cancers of stratified pavement cell epithelium respond very favorably when exposed to roentgen rays and gamma rays of radium, and are cured in a great proportion by reason of the technical progress which has been achieved.

As far as the other pathological varieties of cancers are concerned, the progress of radiotherapy is important to procure temporary remissions of the disease but they have not yet reached, for various reasons, a satisfactory regularity of cure.

The importance of the results obtained cause the institutions, specially designed for the development and teaching of radiophysiology and radiotherapeutic methods, to be considered as vitally necessary and widely remunerative when one views the question from the standpoint of the common good.—*T. Leucutio.*

Huet, J.-A., and Sobel, A. Note sur l'irradiation Roentgen de la région hypophyso-thalamique. (Note on the roentgen irradiation of the hypophyso-thalamic region.) *Bull. et mém. Soc. de radiol. méd. de France*, July, 1930, *18*, 306–308.

Roussy and Camus have demonstrated that there is a direct communication between the pituitary gland and the floor of the third ventricle. Since the regulatory center of the water metabolism (center of the neurovegetative system) is at the level of the third ventricle, the authors believe that some sort of communication between the pituitary gland and the regu-

lation of the water metabolism must exist.

Clinically the relation between the pituitary gland and center of the neurovegetative system is well illustrated by the remarkable results obtained in the sympathetic disorders of menopause by roentgen irradiation of the pituitary gland. Of 40 cases of artificial or natural menopause treated by the authors with roentgen irradiation of the pituitary gland there was disappearance of the sympathetic disorders in 95 per cent of the cases. This suggests that it would be advisable to supplement the induction of the roentgen menopause in every case by irradiation of the pituitary gland so as to relieve patients of the inconvenience of the post-climacteric sympathetic disorders.

The simultaneous effect on the regulatory center of the water metabolism was recently observed by the authors in 2 cases. The first was that of a woman thirty years of age who suffered from chronic diarrhea, vertigo and headaches for a period of eight years. Following opotherapy with ovarian extract, the diarrhea as well as the other symptoms disappeared only to recur within a few days after cessation of the administration of the ovarian extract. In 1928 a roentgen irradiation of the pituitary gland was carried out with the following technique: field 5 cm. in diameter, 10 mm. Al filter, 3 ma., 700 R, temporal field. The first treatment resulted in an immediate cessation of the diarrhea lasting for a period of four months. Following two additional irradiations with the same technique, one over each temporal region at ten days' intervals, the diarrhea and all symptoms ceased permanently. In the second case, that of a man forty years of age, there was a spasmodic coryza associated with very abundant rhinorrhea lasting for a period of twenty years. Following the administration of four roentgen irradiations, given eighteen days apart, with a dose and technique similar to the one above, there was a complete healing of therhinorrhea lasting now for a period of over two years.

These 2 cases are interesting since they prove that roentgen therapy acts not only on the pituitary gland but also on the regulatory center of water metabolism. No final conclusions can be drawn as yet but the authors are carrying out a number of experiments on animals in order to study more precisely this close relation which seems to exist between the pituitary gland and the regulatory center of the water metabolism.—*T. Leucutia.*

Delherm, L., and Beau, Henri. La radiothérapie du sympathique dans certaines affections cardio-vasculaires. (Radiotherapy of the sympathetic in certain cardiovascular affections.) *J. de radiol. et d'électrol.*, July, 1930, *14*, 391–401.

The authors studied the effect of radiation therapy in the following cardiovascular affections. 1. *Vascular disorders:* (*a*) Raynaud's disease. Seven cases in which amelioration was obtained are briefly described. The irradiation was given over the cervicodorsal region and more recently also over the peripheric nerves; (*b*) arteritis obliterans. The results obtained in this condition were already published by the authors in other articles (see this Journal, abs., Jan., 1930, p. 113, and May, 1930, p. 567). Here an additional case is reported in which a marked improvement was obtained following irradiation of the dorsolumbar spine, of the triangle of Scarpa and of the popliteal region; (*c*) other vascular disorders. In an old man eighty years of age with chronic varicose ulcers and a state of hyposystolia, good results were obtained by irradiation of the triangle of Scarpa and of the popliteal region.

In discussing the indications in the above groups, the authors assert that in Raynaud's disease roentgen therapy leads, in addition to cessation of the attacks of syncope and local asphyxia, also to cicatrization of the ulcers, the capillaroscopic examinations showing marked amelioration of the circulation. In arteritis obliterans the irradiation attenuates or suppresses the systolic spasm and produces a dilatation of the collateral vessels, thus leading to cessation of the phenomena of claudication, disappearance of pain and re-establishment of the normal temperature and color of the extremity. In the case of varicose ulcers the amelioration was extremely marked, although no final conclusion can be drawn as yet.

The irradiation was carried out as follows: (1) for the disorders of the upper extremities, on the cervicodorsal region (down to the 2d dorsal); (2) for the disorders of the lower extremities, in the dorsolumbar region (between the 10th dorsal and 2d lumbar), (3) lately, several areas of exposure along the long vessels of the extremity involved being added. Two symmetrical portals were used on each side of the spine, 25 cm. spark gap, 25 cm. focus skin target distance, 5 mm. Al, 400 R per sitting, three sittings per week, 1200 to 1600 R per portal con-

stituting one series, and at least three weeks intervals being allowed between the series. For the direct irradiation of the extremities a lower filter (2 mm. Al) and occasionally a lower voltage were employed.

After discussing the various theories on the effect of the roentgen rays, the authors express the opinion that in the above conditions this is through the intermediary of the sympathetic nervous system. The irradiation probably develops an inhibiting action on the intermediolateral tracts and on the sympathetic ganglions, which leads to re-establishment of the circulatory balance.

II. *Angina pectoris.* Three cases in which a rather satisfactory, though only temporary, amelioration was obtained are briefly described. The effect here also is explained through the intermediary of the sympathetic system. The authors do not believe that roentgen therapy ever results in aggravation of the attacks of certain cases of angina pectoris as claimed by other investigators, as for example Laubry and Chaperon.

The technique of irradiation is the same as for axial sympathetic irradiation except that the roentgen rays are directed to the region of the heart, using one anterior and one posterior portal.

III. *Disorders of cardiac rhythm.* It is well known that in certain cases of Basedow's disease the presternal irradiation, as adjunct to the direct irradiation of the thyroid gland, leads to amelioration of the cardiac rhythm. The same effect is occasionally observed in subjects with a normal function of the thyroid gland but with disturbed cardiac rhythm.

IV. *Arterial hypertension.* The so-called essential hypertension, which according to Vaquez is often due to adrenaloma, occasionally responds favorably to irradiation. In the other types, as nephritis, arteriosclerosis, etc., the effect is less pronounced. In one of the authors' cases with a marked increase of the blood nitrogen, an irradiation of the suprarenals with 1600 R failed to produce any result, but immediate improvement ensued following irradiation of the cardiac region. The headaches disappeared and the patient was able to resume his usual work. Without wishing to draw any final conclusions from this isolated case, the authors express the opinion that the effect was through the intermediary of the sympathetic system.

A bibliography of 44 articles is appended.—*T. Leucutia.*

Chantriot, Pierre. "Un cas de lichen plan, guéri par l'irradiation roentgenthérapique du sympathique." (A case of lichen planus cured by roentgen irradiation of the sympathetic.) *J. de radiol. et d'électrol.*, August, 1930, *14*, 446–448.

A man thirty-two years of age suffering from lichen planus of the thorax, upper extremities, palms and soles and of the buccal mucosa was treated with roentgen irradiation of the sympathetic system; 4 H was administered over each axillary and inguinal region, with 170,000 volts, 2 ma., no filter, treatment being repeated about five weeks later over each supraclavicular and inguinal region. A complete healing ensued except for the lesion of the buccal mucosa, which has failed to disappear.—*T. Leucutia.*

Mahar, and Falcoz. Un cas d'hirsutisme infantile traité par la radiotherapie. (A case of infantile hirsutism treated by radiotherapy.) *Bull. et mém. Soc. de radiol. méd. de France*, July, 1930, *18*, 314–316.

The authors present a case of infantile hirsutism due to hyperplasia of the suprarenal glands following mumps. The condition was treated and improved by roentgen therapy.

Three years ago at the age of seven the child contracted bilateral mumps. This was of a rather benign course. Shortly after the healing of the mumps there was a rapid increase in the weight of the patient with an exaggerated development of the hairy system. The entire body became covered with coarse stiff black hairs, more marked on the back, extremities, upper lip and chin. During the same time there was great change in the character, the child showing signs of advanced maturity. In 1929 mixed opotherapy (thyroid, ovary, pituitary) was instituted, but without much result.

At the age of ten the patient had an abundant growth of black hair distributed over practically the entire body with a mustache and beard. There was no pathologic pigmentation and on palpation there was no evidence of an abdominal or lumbar tumor. The basal metabolism was minus 16. Roentgenograms of the skeleton failed to reveal any pathologic changes. A diagnosis of hirsutism was made (the term first being used by Apert for the designation of a syndrome of obesity and hypertrichosis). It was assumed that the condition was the result of inflammatory changes of the suprarenal glands following mumps.

The application of roentgen therapy with medium penetrating rays (22 cm. spark gap, 0.2 mm. Cu and 1 mm. Al filters) over both suprarenal glands led to remarkable improvement. The treatment was started Feb. 24, 1930, the dose amounting to 300 R given alternatingly over each suprarenal region for a total of six exposures. The series was repeated two months later. The fall of hair commenced shortly after the first treatment and continued for a period of several months. It is noteworthy, however, that the weight, size and arterial pressure remained uninfluenced by the irradiation.

It is difficult to give a satisfactory interpretation of this partial result.—*T. Leucutia.*

Chantriot. Kératodermie et irradiation fonctionnelle du sympathique cutané. (Keratodermia and irradiation of the cutaneous sympathetic.) *J. de radiol. et d'électrol.*, July, 1930, *14*, 415–416.

The author treated a symmetrical palmoplantar non-familial keratodermia (Méléda's disease) in a man thirty-three years of age by irradiating the sympathetic system. The first treatment was given July 26, 1929, over the axillary and inguinal regions, with 175,000 volts, 2 ma., 35 cm. skin target distance, no filter, 875 R. There was a remarkable improvement and for this reason the treatment was repeated on October 2 and November 8. A complete healing resulted.

The good response to the irradiation of the cutaneous sympathetic indicates that certain keratoses, and especially Méléda's disease, must be on a sympathetic basis.—*T. Leucutia.*

Birkett, G. E. The principles of and some results in the radium treatment of buccal carcinoma. *Canad. M. Ass. J.*, Dec., 1930, *23*, 780–784.

Carcinoma at the base of the tongue is the embryonic, undifferentiated, radiosensitive type. Carcinomas of the lip, cheek, floor of the mouth and anterior third of the tongue are of a highly differentiated type and are less radiosensitive. Lesions of the middle third of the tongue, on the tonsils, fauces and soft palate may be either type. All squamous cell carcinomas of the mouth and tongue are radiosensitive, some more so than others.

The primary lesion is treated by radium interstitially, the element being preferred by Birkett to radon. If no glands are palpable no further treatment is given, but the regional lymph drainage is kept under close scrutiny. If glands are palpable, a block dissection is performed and 30 to 40 needles, 20 to 50 mm. in length ane introduced into the cervical region through the operative wound and permitted to remain in place for eight days. External distant irradiation in addition is considered advisable.

The author cites Bemen's results in which he reported 59 per cent of the early cases alive after five years. These were treated by removal of the primary lesion by diathermy followed by insertion of radium needles for twenty-four hours. Regaud, in 1927, reported the following results:

Year	*Total Cases*	*Cures*	*Per cent*
1922	33	6	18.18
1923	54	10	18.50
1924	55	11	20.00
1925	60	17	28.33
1926	54	21	38.88

These include late or inoperable cases as well as the early ones. If a patient survives for three years he has almost an equal chance of surviving five years.

Birkett's results are as follows:

Year	*Total Cases*	*Cures*	*Per cent*
1926	80	18	22.50
1927	74	25	34.7
1928	113	51	45.13

Lane-Claypon, after reviewing the literature, concluded that about 25 per cent of the patients should be alive and well three years following surgical treatment and 20 per cent alive and well in five years. These, of course, include only the operable cases. It is obvious that the results obtained by irradiation which include both the advanced, inoperable, as well as the operable cases, are definitely better.—*J. H. Vastine.*

Quick, Douglas. Radium and surgery in cancer of the tongue. *Canad. M. Ass. J.*, Dec., 1930, *23*, 774–780.

The undifferentiated, highly malignant, anaplastic type of growth which metastasizes early is highly radiosensitive, and irradiation is definitely the treatment of choice. The differentiated tumor which metastasizes later may be treated surgically. In this latter, adult, radioresistant type of growth, response to irradiation is slower, but if the process is con-

trolled, assurance of permanency of the results is much greater. The work of Martin and Quimby established the lethal dose of radiation at 7 to 10 S.E.D. throughout the tumor tissue for the adult type of growth and 3 to 6 S.E.D. for the anaplastic tumor. The maximum dose which can be delivered with impunity to the mid-line of the oral cavity by surface irradiation in a period of two to four weeks is 2½ to 3 S.E.D. Quick concludes that only the most radiosensitive tumors can be cured by surface irradiation. Tumors showing any degree of differentiation require interstitial irradiation. Thus, by microscopic grading of the tumor, Quick contends that the necessity of empiricism has been eliminated.

Treatment consists of biopsy, rigid oral hygienic measures, antiluetic treatment, if indicated, and irradiation—2 mc. gold radon seeds with 0.3 mm. gold filtration being employed interstitially about the primary growth. If the primary growth is bulky, fungating and markedly infected, the implantation of radon is followed in a few days by cautery removal of the condemned area.

Metastasis to the cervical region, which Quick claims is embolic, is treated by radium packs if the primary growth is anaplastic. If the primary lesion is an adult type epidermoid carcinoma, the glands are removed surgically and gold seeds introduced into all suspicious areas at the time of operation. The primary growth is treated by interstitial irradiation with radon seeds. If there is secondary invasion of bone, surgical removal of the diseased bone is indicated.

Carcinoma of the base of the tongue deserves special mention. It is usually anaplastic and very responsive to irradiation. Its location presents a hopeless surgical problem.

Results—reported in Stockholm in 1928.

473 cases of lingual carcinoma treated.

18 per cent present no clinical evidence of disease.

69 per cent are dead.

189 cases without palpable lymph nodes—66 are living without evidence of disease.

161 cases with gross node involvement—6 are living without evidence of disease.

103 cases developed nodes during treatment—12 are living without evidence of disease.

—*J. H. Vastine*

Cade, Stanford. The radium treatment of cancer of the tongue. *Canad. M. Ass. J.*, Dec., 1930, *23*, 771–774.

Radium treatment of carcinoma of the tongue has made rapid strides in the past few years, following the report of the technique and results by Regaud.

The treatment employed by Cade consists of interstitial irradiation of the primary lesion by long radium needles containing 0.6 to 1.3 mg. of radium. These have a screening value of 0.5 mm. of platinum and are left in position in and about the primary lesion for seven to ten days.

One hundred and sixty-nine cases of lingual cancer are reported in which a disappearance of the primary lesion was effected in 126, or 74 per cent. Of these, 43 subsequently recurred locally. The local recurrences occurred more frequently in the cases in which radon seeds were employed. For interstitial irradiation, Cade strongly prefers needles to seeds.

The cervical region is treated routinely. In the absence of palpable cervical glands either irradiation with a radium collar or interstitial irradiation is employed. The latter by the "closed method" i.e., introduction of radium needles directly through the skin about the entire submaxillary and submental regions. In the presence of small, mobile glands, either interstitial irradiation by the "open method" is employed, or a block dissection of the entire cervical region is performed surgically. If these glands prove to be malignant, the operation is followed in two to three weeks by surface irradiation employing a Columbia paste collar, the primary lesion, of course, being treated by "needling" in all cases.

In the cases with extensive, large, inoperable glands, needles are introduced into and about the glands and entire cervical region. This is followed in two to three weeks by surface irradiation. Palliation is all that is usually anticipated in these advanced cases although an occasional miraculous response is seen, which justifies the procedure.

Of the 169 cases, there are 73, or 47.9 per cent alive and free from visible or palpable evidence of disease. The significance of these results is increased when it is considered that there were palpable glands in 130 of the 169 cases and that 83 of them were advanced, inoperable cases. Of 73 survivals, 62 are of two years', or less, duration. The intervention of additional time will be necessary to permit conclusions.—*J. H. Vastine.*

Raynal, Albert. L'irradiation de l'excavation par la voie périnéale. (Irradiation by

the perineal route.) *J. de radiol. et d'électrol.*, July, 1930, *14*, 413–414.

The author describes briefly a chair which is accommodated to deep roentgen therapy by the perineal route. The chair has an opening 13 ×18 cm., the rest being protected by 4 mm. lead. The chair is built rather high so that the deep therapy tube may be placed underneath it.

The apparatus is of value in the irradiation of carcinoma of the cervix (by adding a fifth perineal field to the four transabdominal fields), in carcinoma of the rectum (the perineal field being associated with a sacroiliac and two converging transabdominal fields), and in fibromas.

In using this additional portal of entry one must pay great attention to the increased radiosensitivity of the skin in the perineal region.—*T. Leucutia.*

Lacassagne, A. Les indications de la radiothérapie des sarcomes. (Indications of radiotherapy of sarcomas.) *Arch. Inst. du Radium de l'Univ. de Paris*, 1930, *2*, 247–272.

Summary. Sarcomata constitute a group of cancers in which definition has continually varied and on which the different anatomopathologists cannot agree. At present there is a tendency to place among sarcomata all the malignant diseases of the blood as well as of the supporting and contractile tissues.

Even the histologic examination of sarcomata often presents great difficulties in differentiating between malignant and benign tumors or between a neoplasm and an inflammatory process. Moreover, there exists a large group of unclassified affections which are on the borderline between sarcomata and inflammations.

The pathologic characteristics (variability of site, deep-seated origin, frequency of metastases) together with the great variation in the radio-sensitivity of different types of sarcomata, makes the determination of therapeutic indications very difficult. Often a palliative treatment is all that can be given.

The therapeutic indications are discussed for: (*a*) the sarcomata of the blood-forming tissues (lymphoid and myeloid sarcomata) and (*b*) the sarcomata of the supporting connective tissues (sarcomata of the soft parts and of the skeleton). In the first group radiotherapy (preferably by roentgen rays) is recommended, while in the second one may resort to surgery, especially when this can be performed widely and without causing too much mutilation. In the sarcomata of the limbs, one should attempt radiation therapy before amputation or desarticulation.—*T. Leucutia.*

Milani, Eugenio. La roentgenterapia nelle malattie del sistema emopoietico. (Roentgen treatment in diseases of the blood-forming organs.) *Arch. di radiol.*, Mar.–Apr., 1930, *6*, 379–422.

Diseases of the hematopoietic system are classified into those of the myeloid system, the lymphatic system, the reticulo-endothelial system, the spleen, the white corpuscles, the red cells and the platelets. The technique of roentgen irradiation for these various diseases is given in considerable detail.

Chronic myeloid leucemia is characterized by enlargement of the spleen, often accompanied by weakness and hemorrhage. Some authors irradiate the spleen in this disease and some the bones and liver. Some give fractional irradiation, while others prefer intense irradiation at a single dose. Fifty per cent of the patients are so greatly improved that they can return to work, as compared with 6 per cent by other methods. The spleen is decreased in size and the fever, headache and weakness cured. It is questionable whether life is prolonged, though it apparently is in some cases. The author believes that the prolongation of life depends on the type of blood in the given case. When mature forms and polynuclear leucocytes predominate, the results of roentgen treatment are better. Statistics show that the results are better in myeloid than in lymphatic leucemia. In lymphatic leucemia it is the lymphatic glands that are enlarged and they are irradiated instead of the spleen. Often when one gland group is irradiated, the others decrease in size also. As in myeloid leucemia, after an initial period of oscillation, there is a decrease in the number of lymphocytes, though they always remain relatively high and generally this is accompanied by an improvement in the anemia and in the function of the hematopoietic tissue.

Acute leucemia resembles an infectious septic disease and is generally fatal in three to five weeks. Roentgen treatment is not indicated for if not given with the greatest care it may hasten death. In aleucemic lymphadenosis—the old name of pseudoleucemia is not correct and in-

cludes a number of different types of lesions—some good results, with prolongation of life, have been reported, but a number of authors report very little effect.

Among tumors of the hematopoietic system those in which roentgen therapy has been most used are lymphosarcomas. On account of their histological structure they are very sensitive to irradiation. The latent period in the reaction is very brief. Cases of cure from irradiation have been reported but spontaneous cures and cures under arsenic have also been reported. But even if there is not definite cure in roentgen therapy there is improvement in the signs of compression and improvement in the general condition, and life may be prolonged for some years. The radiosensitiveness of the tumor should be tested with small doses at first for if there is too great destruction of cells there may not only be a violent reaction but also edema of the tumor with increased signs of compression.

Malignant lymphogranuloma is a chronic inflammation of the stroma of the glands. The generally accepted opinion is that radiotherapy may relieve the patient's condition but only rarely prolong life. But cases have been reported in which life was prolonged two to four years.

Roentgen treatment is not indicated in the form of hyperplasia of the hematopoietic system by Isaac and Goldschmidt, in Gaucher's disease or Pick's disease.

Infectious lymphomatosis may be caused by acute diseases or by chronic ones, such as tuberculosis and syphilis. Radiotherapy is effective in the localized forms, particularly the ones caused by tuberculosis.

Among diseases of the erythrocytes, radiotherapy has been tried in pernicious anemia in the form of irradiation of the spleen or the bone marrow. Good results have been reported from the use of stimulant doses of $\frac{1}{4}$ to $\frac{1}{5}$ of a skin unit dose. Irradiation of the spleen has been tried in congenital hemolytic icterus but the results were temporary. Radiotherapy is not indicated in the anemia of acute hemolysis except in malaria in which the attacks of hemoglobinuria are often caused by quinine. In chronic malaria radiotherapy decreases the size of the spleen. In recurrent or quinine-resistant forms radiotherapy alone brings about cure in 25 per cent of the cases and a combination of quinine and radiotherapy in 50 per cent. In symptomatic anemias or ones secondary to toxic substances such as lead, benzoin, etc., irradiation in small doses on the flat bones or the epiphyses gives good results. But these patients generally recover without treatment after the hemorrhage has stopped. Irradiation of the spleen helps to stop the hemorrhage itself.

Polycythemia may be divided into the true form, or Vaquez' disease and symptomatic forms. Radiotherapy is indicated in Vaquez' disease but not in the secondary forms. In addition to improving the condition of the blood, it cures the headache, dizziness and hemorrhage. It has been accused in some cases of bringing about leucemia but there are transition forms from Vaquez' disease to erythroleucemia. Leucemia might be brought about in the treatment of polycythemia by improper technique injuring the myeloid tissue. In leucemias with hemorrhagic diathesis radiotherapy makes the condition worse. Different bones may be irradiated, making frequent examinations of the blood to see that too large a dose is not given.

There are a number of forms of hemorrhage due to defect of the platelets. Radiotherapy has been tried in hemorrhagic diathesis and in hemophilia. After irradiation of the spleen there is an increase of the thrombocytes and the coagulability of the blood returns to normal. Good results have also been reported in rheumatic purpura. The majority of authors think irradiation destroys the cells of the pulp and sets free thrombokinase. Radiotherapy has not been tried in Barlow's disease but it has given brilliant results as a prophylactic before surgical operation; when the spleen is irradiated with $\frac{1}{4}$ to $\frac{1}{3}$ of a skin unit dose operative hemorrhage is reduced to a minimum.—*Audrey G. Morgan.*

Juul, Jens. Significance of the time factor in radium irradiation. *Acta radiol.*, June 30, 1930, *11*, 226–236.

In previous experiments in the roentgen irradiation of mouse carcinomas, the author found that with the same total dose the strongest effect on the tumor was obtained by giving the irradiation in a single massive dose. But the best therapeutic result, that is, the most favorable proportion between skin effect and tumor effect, was obtained by fractional doses, because the skin is also most intensely affected by the massive dose. In this article he reports similar experiments to determine the

effect of radium irradiation of varying intensity and duration. With the same product of intensity and time, a stronger effect on the tumor was obtained with a great intensity in a short time than with a small intensity for a long time. But as the skin is also most affected by the intense irradiation it does not necessarily follow that the intensive irradiation is the most expedient in therapy, as the object of treatment is to obtain the most favorable proportion between the effect on the tumor and the effect on the normal tissues. The experimental technique used did not show definitely which is the best method, but the author is inclined to believe from clinical experience that the protracted method is best, both in roentgen and radium therapy, except in cases, such as small epitheliomas of the skin, for instance, in which massive treatment gives such good results as to make further improvement improbable. Experiments have shown that large doses of radiation given within a brief period are injurious to the organism and may lower its resistance to cancer. Several authors who have previously used the massive irradiation method have now changed to the more protracted method because they found the clinical results better with the latter method. In changing from the massive method to the protracted method it is of course necessary to increase the dose or the effect will be lessened. But the increased dosage is made practicable by the smaller effect on the normal tissues. With reference to the primary skin reaction in irradiation with hard roentgen rays the dose may be increased by about one-third when it is distributed over five days and by about two-thirds when it is distributed over ten days without producing a stronger skin reaction.—*Audrey G. Morgan.*

MISCELLANEOUS

Kantner. Die Röntgenuntersuchung in der Technik. (The roentgen examination in technology.) *Fortschr. a. d. Geb. d. Rontgenstrahlen*, June, 1930, *41*, 873–892.

Although Roentgen in his original paper suggested that the roentgen rays might be used advantageously in the different branches of industry, the practical application of such a procedure is of only recent origin. The author, an engineer in the employ of the German State Railways, has carried out a number of investigations with regard to the value of the roentgen rays in detecting flaws or faulty construction of various machines and has found that the following methods are of especial value:

For the study of the coarse structure of the material used in the construction of various machines one might employ the roentgenoscopic examination which is based on the same principles as that used in medicine, and the roentgenographic examination which, because of the large dimension of the pieces to be examined necessitates a special, rather heavy apparatus. Several of these apparatus are described and illustrated by photographs. One of them is a portable unit mounted in a boxcar. The exposure time for some of the metals used was experimentally determined, the figures being as follows: 200 kv. constant, 4 ma., 40 cm. focus distance, double intensifying screen.

Lead	5 mm. thickness	120 min.
Copper	65 mm. thickness	240 min.
Steel	100 mm. thickness	360 min.
Iron	120 mm. thickness	320 min.
Aluminum	400 mm. thickness	180 min.

The author also studied the value of the stereoscopic examination for the determination of the exact location (whether near the surface or deep) and of the densographic examination for the determination of the exact size and nature of the flaws, and found that both methods are of considerable practical importance.

The fine structure of the materials used was studied by means of the procedures employed in crystallography (Laue). It was found that if during the course of the preparation of the material (by melting, forging, fusing, etc.) a change in the internal tension develops, this can be very accurately demonstrated by the Laue method (Laue diagrams, texture diagrams). The apparatus necessary for the study of the fine structural arrangement of the materials are considerably smaller and therefore they may be used with greater ease.

A third method of investigation, that of the roentgen chemical analysis, still belongs to the domain of laboratory investigation. This method consists either in the determination of the absorption of roentgen rays of certain wave length (absorption analysis) or the determination of the emission of characteristic secondary radiation by the various metals (emission analysis). It is hoped that in the near future a practical application may also be made of this very important method of investigation.

The article is richly illustrated with photographs and diagrams.—*T. Leucutia.*

Chantraine, H. Ueber den Verstarkungsschirm bei Lungenaufnahmen. (On the intensifying screen in lung exposures.) *Fortschr. a. d. Geb. d. Rontgenstrahlen*, July, 1930, *42*, 108–115.

The author investigated the definition of various intensifying screens by exposing to radiation the cross-section of a tarsal bone of the calf under well-established conditions. A filter of 7 to 8 mm. Al was used so as to give roentgen rays similar to those used in the examination of the chest. It was found that the Radiologie and the Patterson screens gave the best definition, though they were somewhat slower, necessitating a longer exposure.

It was found that there are three disturbing factors in the roentgenography of the lungs which must be taken into consideration: the loss of definition due to the use of the intensifying screen, the unsharpness of the lung structures due to thier varying distance from the film and the movement of the lung structures as a result of the heart beat.

While the author previously was against the use of intensifying screens, he now admits that the time factor leading to extremely short roentgen exposures is the more important. In this respect very sensitive films should prove of great advantage. It seems that in the future the competition will be between the very sensitive intensifying screen and the ultrasensitive film. Should the manufacturing of this latter succeed, the use of the intensifying screen may be entirely abandoned.—*T. Leucutia.*

Boldingh, W. Hondius. Ein Verfahren sur Prufung des Entwicklers. (A method of testing developer.) *Acta radiol.*, June 30, 1930, *11*, 217–223.

If it is desired to take a roentgen picture with as short an exposure time as possible with a given focus-film distance, the tube must be as highly charged as possible. If the greatest sharpness is desired with a given time of exposure the focus must be made as large as possible with the charge that can be used. The greatest sharpness of detail can be obtained only by charging the tube highly. But even if the picture is taken properly it may be spoiled in developing. If a poor developer is used exposures three or four times as long as those required by a good developer may be needed. If tension could always be measured simply and reliably and if the same parts of different patients' bodies did not show individual variations, it would be possible to determine a definite time of exposure for every part of the body with a given focus distance and given charge, and an under-exposed picture would indicate at once that something was wrong with the developer. But this is not true so that defects in the developer are often overlooked. There is no chemical test for developer; the only possible test is the photographic method. The author describes his method of testing developer with small packets of films exposed to standard roentgen radiation of a given hardness. If the films of a given firm are used the developer made by the same firm should be used. The developer should be tested once a month.—*Audrey G. Morgan.*

Maino, Mario. L'esame radiologico come mezzo di diagnosi di morte. (Roentgen examination as a means of diagnosing death.) *Radiol. med.*, May, 1930, *17*, 544–558.

Of all the methods of diagnosing death a study of the circulation is the most reliable. There cannot be death without total and prolonged arrest of circulation. Icard's fluorescin test is based on this principle. Maino first gives a critical discussion of what has been done in this field by various authors. The technique which he uses in case of apparent death is as follows: About 3 c.c. of potassium iodide is injected into the cephalic vein at the bend of the elbow and a roentgenogram made of the arm after a certain length of time to see whether the injected liquid remains immobile; if it does it is a certain sign of death. This method is simple and absolutely certain and the contrast substance is perfectly harmless.—*Audrey G. Morgan.*

Turano, Luigi. Sulle modificazioni dei capillari alle radiazioni Röntgen. (Changes in the capillaries on roentgen irradiation.) *Arch. di radiol.*, Mar.–Apr., 1930, *6*, 349–363.

Early in roentgen therapy it was noticed that different individuals react very differently to the same dosage of rays; erythema is much more intense in some than in others with the same dosage. It was found later that the radiosensitiveness of the individual could be tested by examination of the capillaries. There are

two chief theories in regard to the function of the capillaries: one that they are influenced by chemical agents and the other that changes in their caliber are brought about by their own intrinsic nerves which are under the control of the vegetative nervous system. The author gives illustrations of the appearance of a normal capillary and then of ones that have suffered varying degrees of roentgen injury extending from simple erythema through roentgen epidermitis to roentgen dermatitis. The normal capillary shows the picture of a granular current, arrested here and there momentarily and then continuing its course. The background is yellow or yellowish red. Pathological capillaries differ from this picture in number, form, color of the background and the fact that the subpapillary reticulum, particularly the deep one, cannot be seen. There may be an unusually large number capillaries and there may be fields where there are practically none at all. If there are more capillaries than normal it means that they are dilated and this has brought into view reserve capillaries that are generally not filled. When there are few or no capillaries it means that their walls are in a spastic condition, provided they have not been destroyed. This renders the individual more sensitive to irradiation. When the sympathetic system predominates, the capillaries are spastic and when the parasympathetic predominates, they are dilated and the reserve capillaries are filled. The background is also much redder when the capillaries are abnormal, due to vasodilatation of the superficial and deep subpapillary reticulum. When the capillaries are spastic the background is pale.

Examination of the capillaries furnishes a means of controlling roentgen therapy and telling when it should be stopped as the changes in the capillaries always precede the macroscopic changes on the skin. It is also possible to determine the individual's roentgen sensitiveness in advance by means of capillaroscopy. Welsch proposes making a preliminary test with ultraviolet rays to determine the sensitiveness of the capillaries; this indicates the way in which they will react to roentgen irradiation. He found that patients with vasoneurosis, nephritis, Basedow's disease, etc., showed intense vasodilatation. The author tested this reaction to see whether the patients did react in the same way to roentgen irradiation as to the preliminary ultraviolet test and found that they did.

These observations are interesting as showing that the capillaries have an autonomous nervous system, that individuals with disturbances of the vegetative nervous system are more radiosensitive than normal ones and that the alternating phases of constriction and dilatation explain the waves which Miescher saw in the course of roentgen erythema.—*Audrey G. Morgan.*

Ko Muro-Hide o. Mikrochemische und zytologische Befunde an röntgenbestrahltem Pflanzengewebe. I. Ueber "tiefgefärbte zytoplasmatische Zellgruppen" im Wurzelspitzengewebe von Vicia faba. (Microchemical and cytologic findings in tissues of plants irradiated by roentgen rays. I. On "deep-stained cytoplasmic cell groups" in the tissues of root endings of *Vicia faba.*) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1930, *41*, 948–949.

It is a known fact that the cytoplasm does not take the basic hematoxylin, unless pathologic alterations change its reaction to acid. The author irradiated the seeds of *Vicia faba* with roentgen rays (74,000 volts, 5 ma., 17 cm. distance, 2 hours) and noticed that after germination there were in the periblem of the growing points of shoots, near the plerom, deep-stained cytoplasmic cellular growths which have stained well with the hematoxylin. It was thought that these changes were due to the acid reaction produced by the roentgen rays. The cell groups have also shown the characteristic reaction with ruthenium red, a fact which indicates the presence of pectin substances.

Since the plasma of the plants contains protein, fat, carbohydrates, P, Fe, Mg, etc., it is the author's contention that the carbohydrates have been transformed by hydrolysis into galactose and pentose, this latter giving the characteristic reaction with ruthenium red. It appears that the cytoplasmic density along the cell wall which the author wishes to call the marginal layer and which most probably consists of colloidal deposits of cytoplasmic constituents, is of paramount importance for the life processes of the cells. The cellulose constituents of the cell wall are from this standpoint of no importance.—*T. Leucutia.*

Mutscheller, A. Durchschnittliche Quantenenergie. Eine Methode, sie zu messen, und deren Beziehung zur biologischen Wirkung der Röntgenstrahlen. (Average quan-

tum energy. A method of measuring it and its relation to the biological action of roentgen rays.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1930, *41*, 899–904.

The introduction of the r-unit has been delayed because it is physically not easily reproduced. A method is herein described with which, by means of an instrument that does not require standardization, it is possible to measure the average energy of the radiation quanta. If the radiation is filtered down to 10 per cent of its initial intensity, then calculation shows that for an r-unit there are necessary 0.508×10^8 quanta. A dosimeter can be recalibrated without standardized instruments, since the milliammeters ordinarily used are sufficiently accurate.

The quantum point of view is much simpler and clearer, not only for the scattering hypothesis but also as regards the visualization of the action of roentgen rays upon tumor cells. It would really be an advantage if the wave idea were abandoned. The possibility of determining the average energy of quanta by a simple measurement would greatly simplify the entire problem of roentgen therapy. Furthermore, it would aid to clarify the complicated relation between the biological effects upon the tumor cells and upon the skin.—*T. Leucutia.*

Zimmern, A., and Chavany, J. A. La radiosensibilité des tissus nerveux. (The radiosensitivity of nervous tissues.) *J. de radiol. et d'électrol.*, August, 1930, *14*, 433–441.

The nervous tissues occupy in "the spectrum" of radiosensitivity of normal tissues a position which is at the opposite end from that of the white elements of the blood, of the lymphatic tissue and of the active elements of the reproductive organs. As is known, the encephalon, the spinal cord and the peripheral nerves can be exposed to large doses of roentgen rays without the least organic alteration. Even during the stages of actual development the nervous tissue remains very resistant to radiation.

This relative immunity disappears, however, as soon as there is pathogenic involvement. In syringomyelic gliosis, for example, there is a marked sensitivity to roentgen rays; it is possible that the effect is indirectly through the changes brought about in the vascular system supplying the nerve tissue. The cerebral tumors which in the majority of instances are primary neoplasms, show a radiosensitivity which is varying according to the structural composition. Thus in the group of the gliomas, the medulloblastomas because of their lesser differentiation and the preponderance of the cellular elements are more sensitive to radiation than, for example, the astrocytomas, which show a very slow, highly differentiated course. The meningiomas, schwannomas and neurogliomas, being derivatives of elements of adult nerve tissue, are extremely radioresistant. Of the pituitary tumors, the eosinophile adenomas, which are associated with acromegaly, are likewise very radioresistant and so are most of the extrasellar tumors (fibromas, teratomas, meningiomas, cysts) and the tumors originating from the pouch of Rathke.

As is known, the roentgen rays have a destructive or an inhibiting action on the various tissues. This effect can be advantageously used in the treatment of various neoplasms of the nervous system. One should bear in mind, however, that large doses although without effect on the nervous elements may produce alteration of the vascular system and choroid plexus, giving rise to a rather pronounced reaction. Thus one observes not infrequently headache, vertigo, vomiting, disorders of equilibrium, Jacksonian crises and especially visual disturbances, followed occasionally by somnolence, coma and even death. The mechanical consequences of this reaction, which is best called pre-reaction, are especially pronounced in the presence of increased intracranial pressure.

In addition to the cancericide and inhibiting action, the roentgen rays also possess a certain power to dissolve inflammatory processes (Heidenhain and Fried). This effect can be exploited with success in the treatment of neuralgias (sciatic, brachial plexus, etc.) as well as of certain arthritic lesions of the vertebrae (radicular radiotherapy).

Finally, certain clinical observations seem to point to the fact that the roentgen rays have a direct or intermediary action on the vegetative system (treatment of lichen planus, angina pectoris, intermittent claudication, hypertension, etc.).

The action of the gamma rays of radium is similar to that of the roentgen rays, except that certain tumors appear more sensitive to the influence of the radium than of the roentgen rays. This phenomenon permits occasionally the successful application of radium to radioresistant tumors formerly treated by roentgen rays.—*T. Leucutia.*

Gricouroff, Georges. Etude histologique de l'action des rayons X sur l'ovaire a la période d'ovogénese. (Histological study of the action of roentgen rays on the ovary during the period of ovogenesis.) *Arch. Inst. du Radium de l'Univ. de Paris*, 1930, *2*, 1–80.

Summary. The mammalian ovary is very sensitive to the action of the roentgen rays during the period of ovogenetic activity (multiplication of the ovogonies and nuclear differentiation of the ovocytes). A single irradiation, correctly administered, can produce the total and definite destruction of the sexual elements.

The diminution in volume of the ovary is early and rapid. Eight days after the irradiation the regression of the cortical zone is achieved. On the fourteenth day the medullary zone being considerably diminished, the ovary becomes reduced to a thin fibrous layer.

The first effect, detectable one hour after irradiation, consists in the arrest of caryokinetic multiplication of the epithelial and connective tissue cells, and the destruction of the mitoses. Especially the multiplication of the ovogonies is completely arrested.

The elements of the sexual chain are affected in an elective manner. The ovogonies, particularly sensitive, manifest changes from the first hour. At the end of twenty-four hours they are almost completely destroyed. The ovocytes are more resistant and their alteration more delayed. The topographical repartition of the changes of the primitive cortical zone permits the evaluation of the relative sensitivity of the ovocytes: the older the ovocyte and the better the differentiation of its nucleus, the more radioresistant.

If the irradiated ovocyte is not entirely destroyed, it will continue its evolution in routine fashion, the nucleus preparing itself for this chromatic reduction with the same rhythm and passing through the same morphologic stages as the normal ovocyte.

No new formation of ovocytes will take place from the undifferentiated cortical elements which have escaped the action of the rays. Ovogenesis is definitely checked.

The follicular cells, which cannot be distinguished from the ovogonies by their structure, have a relatively slight sensitivity, a certain number persisting among the last epithelial elements of the cortical zone.

There exists a manifest radiophysiological parallelism between the homologous stages of the male and female sexual chains. The germinal cells (spermatogonies and ovogonies) have an extreme and very characteristic sensitivity. The spermatocytes and ovocytes of the first order, less sensitive as a whole, become more and more resistant as they progress in their differentiation. The rhythm of evolution is not altered by the irradiation in any of the two chains.

The medullary zone of the ovary is little damaged by the direct action of the roentgen rays. Nevertheless it eventually disappears as if "stifled" by the sclerosis of the connective tissues produced by the irradiation.

The ovarian connective tissue shows active proliferation at the moment of the irradiation. One hour later the mitoses cease. Cytolysis starts from the second hour, especially in the loose connective tissue of the medullary zone. The alteration progresses, until the sixth hour, then diminishes, leading to gradual sclerosis. Fourteen days after irradiation, the cortical zone is entirely sclerosed, the medullary zone being occupied by lymphatic vacuoles.

The alteration of the connective tissue under the influence of roentgen rays in a young ovary contrasts with the integrity of the adult ovary and testis.

The vascular endothelium of capillaries as well as of larger vessels does not present, after irradiation, any changes which can be detected histologically.

In the uterine tube, one observes changes as early and as intense as those in the ovary. They pertain to all layers, are of only temporary duration, beginning to disappear within six hours, and are followed by reparation starting from the sixth day. By the twelfth day the development of the tube has again become normal. The changes of the tube are thus contrary to those of the ovary by their non-selectivity and their temporary character. Starting from the sixth day, the active development of the tube coincides with the complete regression of the ovary. One must conclude therefore that at this stage, this portion of the genital tract is independent of the presence or absence of sexual elements or of secretions of ovarian hormones.—*T. Leucutia.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE GASTROINTESTINAL TRACT

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

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CONTENTS

PREFACE

GENERAL CONSIDERATIONS 1

ORAL MUCOUS MEMBRANE 1

- Animal Experiments 1
- Clinical Considerations 2
- Conclusions 2

TEETH 3

- General Considerations 3
- Animal Experiments 3
- Analysis of Experimental Data 4
- Clinical Considerations 5
- Conclusions 6

SALIVARY GLANDS 6

- Animal Experiments 6
- Analysis of Experimental Data 11
- Clinical Considerations 12
- Conclusions 16

ESOPHAGUS 16

STOMACH 17

- General Considerations 17
- Animal Experiments 17
- Analysis of Experimental Data 30
- Clinical Considerations 35
- Conclusions 39

(To be Continued in the August Issue)

PREFACE

Strange as it may seem to the initiated, the existence of a scientific foundation for radiotherapy is even now being questioned. In a recent editorial in the *Lancet** it was stated that "there is still an uncomfortable amount of truth in the gibe that the whole of radiology in its radiotherapeutic aspect lacks scientific basis and rests largely on an empirical footing." It must be admitted that many problems relating to radiotherapy are still the subject of controversy and that the large number of experiments which have been made have yielded only partial answers to many questions. Nevertheless, the experimental facts already established are sufficiently numerous to provide an adequate, although incomplete, scientific background.

Before the action of roentgen rays and radium on pathologic lesions can be understood it is essential to know the action of such rays on normal cells and tissues. The object of this work is to bring together the available experimental and clinical evidence and to subject this material to close scrutiny with a view to extracting from it the essential information about the effects of roentgen rays and radium on normal tissues and organs. The method adopted has been to prepare a careful and complete abstract of each original report, as published by the experimenters themselves, including every item of essential information therein contained. Every effort has been made to preserve as much as possible the meaning of the authors of such reports, even to the point of preserving ambiguous statements when such statements were present. These abstracts have been arranged in chronologic order to facilitate reference and enable the reader to follow the historical development of the subject. The experiments with roentgen rays have been grouped separately from those with radium. These two groups of experimental reports have then been subjected to critical analysis, and this follows the experimental reports themselves. The analysis, in turn, is followed by the clinical considerations, in which is taken up the therapeutic application of roentgen rays and radium to every disease in which the particular tissues or organs are affected. Finally, all the data, experimental and clinical, are correlated and summed up.

Although the greatest care has been taken to make this study as complete and as thorough as possible, I am conscious that errors, discrepancies, and oversights must have occurred. Certain experiments may unwittingly have been omitted. The opinions expressed are my own and for these I hold myself responsible. It is probable that, as time goes on and as fresh material becomes available, some of the deductions and conclusions may have to be modified. As far as the clinical considerations are concerned, it has been impossible to mention every report which has appeared in the literature, because this would have involved long lists of names which must serve only to tax the patience of the reader. In dealing with this phase of the subject, I have taken pains to include every author of importance and to give to each country due representation in proportion to the number of communications emanating from it. In this way, it will serve to indicate the country in which certain phases of radiotherapy have been most highly developed. The bibliography is substantially complete, although a few items which could not be procured have been omitted. I will appreciate having my attention drawn to any significant omission.

Rochester, Minnesota,
March, 1931.

*Lancet, 1931, *I*, 141.

ACTION OF ROENTGEN RAYS AND RADIUM ON THE GASTROINTESTINAL TRACT

General Considerations

CASUAL reading of contemporary medical records bearing on the action of roentgen rays and radium often gives the impression that little is known concerning such action, and the most misleading statements are made and preposterous notions advanced, in spite of the fact that, as far as some phases of the subject are concerned, more or less substantial or conclusive experimental data are available to indicate or to clearly establish the nature of such action. In some cases, indeed, the experimental indications are absolute. In other cases adequate experimental evidence may be lacking, but the clinical data may be sufficient to indicate the probable effect of irradiation. Unfortunately, the evidence furnished by experiments on animals and by clinical reports has never been brought together, analyzed, and correlated, and much of it has been lying on library shelves, buried in medical journals which are seldom read. Heretofore, the magnitude of the task has prevented anyone from attempting to sift this material. Colwell and Russ and a few others have, it is true, examined some of this material and have made valuable deductions, but a thorough analysis and appraisal have never been undertaken.

With reference to the gastrointestinal tract, knowledge of the action of roentgen rays and radium has been confined to a few generalizations, some of which are not warranted. For example, if we may judge by the relative paucity of references, few radiologists appear to realize the exceptional sensitiveness of the salivary glands and to understand the mode of action of the rays. The influence of radiation on the intestine furnishes another instructive example. Certain investigators have claimed that the relative susceptibility of the small intestine, conclusively established by several series of experiments, serves to explain the systemic reaction so common in clinical radiotherapy. As will be shown later, such a conclusion is quite unwarranted, but many radiologists and others have accepted the explanation notwithstanding.

ORAL MUCOUS MEMBRANE

In general, mucous membranes are said to possess approximately the same degree of sensibility to roentgen and radium rays; a sensibility usually regarded as slightly greater than that of the skin. Abundant clinical evidence is the chief ground for this view, since direct experimental study of the specific sensitiveness of such membranes is comparatively limited.

Animal Experiments

CASE and BOLDYREFF (1925), in the course of experiments on the effect of irradiation on the secretory activity of the salivary glands (page 8) noted that, after irradiation, the oral mucous membrane of dogs seemed less sensitive to stimulating substances introduced into the mouth. The authors proceeded to test the validity of this assumption by measuring, before and after roentgen irradiation, the sensitiveness of the mucous lining of the mouth of four dogs by means of a Dubois-Reymond induction coil. The sensibility was found definitely diminished after irradiation. Similar tests on six persons, who had received roentgen treatment at various times, also showed diminished sensitiveness of the oral mucosa as compared

with that of a young person who had not received irradiation. Thus it was indicated that roentgen rays diminish the sensibility of the oral and lingual mucosa, that the mucosa tends to return to normal after an interval which depends on the intensity of irradiation, and that the diminution in sensibility parallels the diminution in functional activity of the salivary glands after irradiation.

Clinical Considerations

If there is but little experimental evidence on the sensibility of the oral mucous membrane to irradiation, the clinical evidence, on the contrary, is quite abundant. Indeed, almost daily every therapeutic radiologist observes manifestations of the effect of irradiation on the mucous membrane of the mouth. Patients irradiated from within (radium) or from without (roentgen rays or radium), for various lesions around the mouth, often complain a short time later of loss of taste and sensation, but these symptoms are so closely associated with disturbance of the salivary glands that differentiation is not easy and is seldom made.

The tissues bounding the oral cavity on both sides are not thick, and the tissues forming the floor of the cavity are only slightly thicker. It is but natural, therefore, that strong external irradiation should influence the oral mucosa almost as much as direct irradiation. Under the circumstances, the quality and quantity of the radiation may not be greatly altered by passage through the tissues of the cheek or floor of the mouth. This is especially true of rays of short wave-length. Hence, a dose of roentgen or radium rays sufficient to cause reaction in the skin is likely to cause reaction also in the mucous lining. Sensation and taste tend to return to normal after a period which depends on the amount of radiation, but, after a strong dose and consequently a marked reaction, the mucous membrane may be slow to recover. It may even ulcerate and heal by granulation, or a telangiectatic area may remain as lasting evidence of local overdosage. Doses that are not sufficient to cause the skin to react do not affect the mucosa perceptibly.

Radiotherapy For Lesions of the Oral Mucous Membrane. Certain lesions around the mouth, such as gingivitis, glossitis, stomatitis, leucoplakia and psoriasis have been treated by irradiation, apparently with some success. Levy (1912 and 1913) called attention to the favorable effect of radium and mesothorium on psoriasis of the buccal mucosa and on other local inflammatory processes, such as gingivitis, chronic ulcer and leucoplakia. Schultze (1919) recorded cases of Moeller's glossitis and chronic gingivitis that improved after exposure to roentgen rays. Cathcart (1923) cited the interesting observation of a patient with gangrenous stomatitis which healed rapidly after a single exposure to roentgen rays. Van Gangelen (1923), Ward (1926) and others have written favorably on the value of radium in the treatment of leucoplakia.

Injury to the Oral Mucous Membrane. Few cases of severe radiostomatitis have been recorded, and most of these have been incidental to the treatment of cancer of the lip, tongue, cheeks and pharynx with radium, but such cases are sometimes encountered after accidental overexposure or repeated strong irradiation with roentgen rays. Such a case was reported by Killian (1920), and many others have undoubtedly occurred but not been recorded.

Conclusions

The experiments of Case and Boldyreff indicate that strong irradiation diminishes the sensibility of the oral mucosa. The recovery of function may be rapid or slow

and complete or incomplete, according to the dose of radiation. This is in harmony with clinical observation, but such evidence is generally confounded with the effect of irradiation on the salivary glands, and will be reviewed in connection with that subject. Certain forms of gingivitis, glossitis and leucoplakia have been successfully treated with radium.

TEETH

General Consideration

The only experiments on animals relating to the action of irradiation on the teeth were conducted by Leist with roentgen rays and also with radium.

Animal Experiments

Leist (1925) irradiated[1] the anterior portion of the head (forehead and snout) of eight rats to ascertain the action of roentgen rays on growing teeth. Five of the rats received 15 Holzknecht units of unfiltered rays, two were exposed five and six times respectively to 1.5 Holzknecht units and then three times to 15 Holzknecht units; one rat received only 1.5 Holzknecht units.

In contrast to the teeth of normal control rats those of the irradiated rats showed that the odontoblasts of the germinal layer of the constantly growing gnawing teeth were greatly injured. The formation of dentin almost stopped after each irradiation, and niche-like projections could be seen in which the pulp extended into the dentin; these niches contained degenerated odontoblasts, large numbers of which had disappeared. The number of niches in the dentin corresponded with the number of exposures to roentgen rays. The signs of injury were much less pronounced after short exposures. The alterations in the odontoblastic layer were sufficiently marked to diminish the rate of growth of the gnawing teeth. No effect on the grinding teeth was observed. These changes were most distinct on the convex side of the upper gnawing teeth, less distinct on the concave side of the upper teeth and still less in the lower teeth, which is accounted for by the general downward direction of the beam of rays. No change in the enamel or cement was noted.

Leist (1926) studied the effect of exposure to roentgen and radium rays on the second dentition of three young dogs that had their milk teeth, forty-one, sixty and seventy-two days before the appearance of the permanent teeth. Two of the animals were exposed to roentgen rays and one to radium; "strong doses were used in order to produce definite changes." The three dogs came from three different litters, and one dog from each litter was used as a control. The right side of the jaw of one dog, which weighed 3 kg., was exposed to 8 Holzknecht units and sixteen days later to 10 Holzknecht units of unfiltered roentgen rays.[2] Twenty-nine days after the second exposure the same animal received an additional exposure to 12 Holzknecht units, and a fourth exposure to 15 Holzknecht units of rays filtered through 2 mm. of aluminium was made twenty-nine days after the third irradiation. Three months after the first exposure, and eighteen days after the fourth and last exposure, the control dog had a complete set of teeth, except for the third molars. The irradiated dog had only eighteen permanent teeth. The control animal was better developed and weighed 1 kg. more than the one irradiated, although both weighed approximately the same at the outset. The delay in dentition of the irradiated dog was greatest on the side nearest to the roentgen tube. Radiodermatitis with edema of the surrounding skin developed, and later ulceration; the appetite was defective, and this probably accounted for the difference in weight between it and the control animal. The right side of the jaw of the second dog which

[1] Voltage, 120 kv.; focal-skin distance, 28 cm.; rays not filtered; current, 3 ma. Neither the age of the rats nor the intervals between the different exposures were given.

[2] Voltage, 120 kv.; focal-skin distance, 28 cm.; current, 3 ma.; The head, with the exception of the jaw, was shielded from direct irradiation.

weighed 1.8 kg.,[3] was exposed to 10 Holzknecht units of unfiltered roentgen rays under the same conditions as for the first animal. A second exposure to 15 Holzknecht units was made twenty-nine days later, and a third to the same dose of rays filtered through 2 mm. of aluminium was made sixty-four days after the second irradiation. There was now a difference in weight of 2,300 grams in favor of the unirradiated dog, the cause of the difference being the same as in the first experiment. Through physiologic variation in the time of dentition, the eruption of the permanent teeth in the irradiated dog started one month sooner than in the control, but the process advanced much more slowly on the side of the jaw nearest the tube.

The right lower jaw of the third dog was exposed to 100 mg. of radium in a glass tube enclosed in another tube of silver. This container was 4.5 cm. long and was surrounded by an outer capsule of platinum 0.3 mm. thick, and gutta percha as a secondary filter. The radioactive source was applied to the right lower jaw for one hour (100 mg-hr.). Twenty-nine days later the same radium source, with an additional filter of zinc,[4] was also applied to the right lower jaw for one hour (100 mg-hr.). A third similar exposure to radium, without the zinc filtration, was made twenty-seven days after the second. The right upper jaw was exposed three times to the same dose of radium at intervals of thirteen and thirty days respectively. The eruption of the permanent teeth began at about the same time in the irradiated and control animals, but three months later there was obvious evidence of delayed dentition in the exposed dog. The process was distinctly slower on the irradiated than on the opposite side, and required much more time in the irradiated dogs than in the normal controls. Moreover, the growth of the permanent teeth in the three irradiated dogs was less complete than in the unirradiated controls; also the growth of the jaw on the side exposed to the rays was distinctly retarded.

The effect of irradiation on the growing teeth of dogs was different from that observed in rats in that inhibition of growth affected the crown and root of the teeth in the irradiated half of the jaw within two and one-half months after large doses. "The odontoblasts were fewer in number, and did not form a regular, thick seam between the dentin and pulp; their shape was greatly altered, their nuclei shrivelled and lying in great confusion." The network of fibers between the cellular remains indicated early reticular atrophy of the pulp. Growth ceased in the irradiated premolar teeth, and they became loose and fell out. Partial cessation of growth and subsequent regeneration or complete cessation of growth and loss of the teeth was found to be purely a matter of dosage. Leist regarded the loss of teeth as due to injury of the periosteum or of the alveolar process itself. The trabeculae of the bone were narrowed, and the marrow had become more fibrous than normal marrow. He concluded that the radiosensibility of growing teeth is much greater than that of teeth in which growth has ceased.

The more intense, though more circumscribed, effect of radium showed that the odontoblasts of mature teeth also may be injured if they are exposed to a sufficiently strong dose (from 2 to 5 erythema doses). Reticular atrophy of the pulp and replacement of the odontoblasts by vacuole-like spaces at the border of the dentin and pulp were constantly noted. The number of the odontoblasts greatly decreased and their nulei were shrivelled. Numerous lipoid phagocytes were noted. The enamel and cement were normal. The injury to mature teeth was more lasting than injury to growing teeth, the latter showing a distinct tendency to regenerate.

Analysis of Experimental Data

If experiments had been limited to the effect of irradiation on the eruption of permanent teeth, one would be inclined to conclude that the retarded and abnormal

[3] The weight of the control animal was the same.
[4] Thickness not specified.

eruption of the second set of teeth after exposure to roentgen rays or radium was probably secondary to deficiency in growth of the jaw resulting from such exposure. Retardation and deficiency in the growth of bones in young animals has been shown experimentally many times; hence, in this respect, Leist's observation of delay and deficiency in the growth of the irradiated jaw confirms the observations of other investigators. However, Leist's investigation of the effect of roentgen irradiation on the gnawing teeth of adult rats indicates that the disturbance in growth is largely due to direct action of the rays on the teeth. The odontoblasts between the dentinoid and dentin layers undergo degeneration, whereas the enamel and cement remain unaffected. This is another example of the inhibitory effect of radiation on actively growing cells.

Clinical Considerations

Pyorrhea Alveolaris. Many reports have been made of the clinical action of irradiation on some of the pathologic processes affecting the teeth. PARKER (1903), PRICE (1904), SATTERLEE (1906), KNESCHAUREK and VON POSCH (1916), GARRETSON (1921 and 1922), ARNONE (1922), VON POSWIK (1923), and others have written favorably on the usefulness of roentgen rays in pyorrhea alveolaris or quoted cases in which the condition had improved or was cured. Garretson believed that the rays caused improvement by acting on the lymphoid elements. Arnone stated that the color of the gums changed rapidly after exposure to roentgen rays. This also indicates diminution in lymphocytic infiltration, because the lymphocytes are the only cells that would react so rapidly to irradiation. TRAUNER (1913), LEVY (1913), NEUMANN (1913), MAMLOK (1913), DAUTWITZ (1913), have claimed that radium in the form of solutions of some of its salts or of radium emanation, in compresses, by injection, or internally, is effective against alveolar pyorrhea. These claims do not appear to have been sufficiently substantiated to command attention. Indeed, PORDES and many others, who have tried radiotherapy in alveolar pyorrhea, did not observe improvement. In view of the nature of the disease, its treatment by roentgen rays or radium must be surrounded with uncertainty. However, many cases reported as examples of the beneficial effect of roentgen rays on pyorrhea really represent action on periradicular abscesses and granulomas. The two cases mentioned by von Poswik (1923) probably belong to this category.

Periradicular Abscess, Granuloma and Phlegmonous Inflammation of the Jaw. The therapeutic efficiency of irradiation against infectious processes around the roots of teeth seems to rest on more solid ground. KNESCHAUREK and VON POSCH (1916), KNOCHE (1920), SCHMIDT (1921), WITT (1921), FESSLER (1922), SCERVINI (1922), LEVY (1922), PHILIPP (1922), STEIN (1926), and especially PORDES (1924, 1925, 1926), have offered tangible, clinical evidence of the salutary effect of irradiation in periradicular abscesses and granulomas, and also in phlegmonous infection of the jaws. These pathologic conditions appear to be influenced rapidly and their resolution hastened by exposure to roentgen rays. The mechanism of this action is apparently the same as that by which irradiation influences furuncle, carbuncle and other inflammatory processes accompanied by marked lymphocytic infiltration. Lymphocytes are known to be exceptionally sensitive to irradiation, which rapidly destroys large numbers of these cells. This explanation, offered by Pordes, is undoubtedly sound and is supported by many experimental and clinical facts.

Injury to the Teeth from Irradiation. Instances of injury to the teeth, supposedly from irradiation, have been reported by GOTTHARDT (1922), and JÜNGLING (1924). In the case cited by Gotthardt roentgen irradiation had been applied to the neck and lower part of the face for tuberculous cervical lymphadenitis. By mistake, this treatment had been carried to such an extreme that marked changes occurred in all the tissues exposed. As shown by Jüngling's case, it is probable that absence of saliva resulting from overexposure of the salivary glands, may have played a significant part in the subsequent changes in the teeth. However, it is also likely that part of these changes are to be attributed to injury and atrophy of muscles and bone.

Leist also has called attention to the possible injurious effect on teeth of exposure of the pregnant uterus to roentgen rays. He cited the case reported by Stettner in which the uterus and ovaries of a pregnant woman had been irradiated for supposed myoma. She gave birth later to an unusually small child who subsequently showed microcephaly and imbecility. Teeth had not appeared at the age of twelve months; eruption was not only delayed, but when the teeth appeared growth was irregular. This may not have been a direct effect of irradiation on the dental apparatus of the fetus, but may have been secondary to the general disturbance in growth and metabolism by prenatal exposure to roentgen rays.

Conclusions

The animal experiments indicate that roentgen rays influence the growth of teeth by inhibiting the development of the odontoblasts and perhaps also by retarding the development of the jaw bones. Even mature teeth may undergo atrophy and fall out on exposure to strong doses of roentgen rays or radium.

Roentgen rays have been credited with therapeutic effectiveness in pyorrhea alveolaris and many cases have been recorded that tend to substantiate the claim. However, the beneficial effect of irradiation has not yet been clearly established.

Irradiation has been shown to have a distinctly salutary influence on periradicular abscess, granuloma, and also on phlegmonous inflammation of the jaw, probably owing to the destruction of lymphocytes infiltrating the inflamed tissues.

Injury to the teeth from exposure to roentgen rays or radium may occur directly from overdosage, but in the recorded instances such injury appears to have been due to absence of saliva from excessive irradiation of the salivary glands. Exposure of the pregnant uterus to radiation has been known to inhibit dental development in the child, but this was probably the result of interference with general growth.

SALIVARY GLANDS

The salivary glands have long been known to be more sensitive to irradiation than the overlying skin or the underlying mucosa of the mouth, but, with few exceptions, those who have observed the effect of roentgen rays and radium on these glands have mentioned it only incidentally in connection with comments on radiotherapy for various lesions around the mouth, face and neck.

Animal Experiments

Roentgen Rays. IVY, ORNDOFF, JACOBY and WHITLOW (1923) investigated the late effect of irradiation on the submaxillary gland of six dogs after the preliminary operative establishment of a salivary fistula of Wharton's duct, and after determining the continuous secretion and the salivary response to standard stimuli, such as 0.5 per cent solution of hydro-

chloric acid applied to the oral mucosa for one minute, the eating for two minutes of roast beef salted to taste, and the hypodermic injection of 5 mg. of pilocarpin hydrochlorid. The response to these preliminary tests was within the range of normal variation. The saliva was collected and measured, and chemical determinations of the total and of the inorganic and organic solids were made on each quantum of secretion collected. The viscosity was determined by the Ostwald pipette method. The hydrogen ion concentration was ascertained by the colorimetric method, with phenolsulphonphthalein as indicator. Determinations of the salivary diastase also were made. Three different doses of roentgen rays were chiefly employed, but in some of the experiments other, intermediate, doses were used.[5] The necessity of keeping the animals anesthetized for from two to three hours made it necessary to run parallel control experiments on unirradiated animals to determine the effect of the experiment itself on the output of saliva and on the volume of blood flowing through the gland. Thus it was found that the experimental conditions themselves caused a 26 per cent reduction in the secretory response of the gland, no reduction in the continuous volume flow of blood through the gland, and a 31 per cent reduction in the volume flow of blood after stimulation of the chorda tympani nerve for ten seconds every fifteen minutes for two hours. One gland was irradiated while parallel determinations on the other gland served to control the results and to measure the effect of the experimental conditions per se.

Small doses of roentgen rays did not cause any immediate increase in the continuous flow of saliva from the irradiated glands, and did not sensitize the glands to subsequent nervous stimulation. Large doses diminished the immediate response of the gland to nervous stimulation and to injection of pilocarpin. Constant, immediate variation in the chemical composition of the saliva was not observed. Small doses of unfiltered roentgen rays had no immediate effect on the blood volume flow. Large doses had an apparent vasoconstrictor action on the blood vessels and caused the blood volume flow to decrease as the result of passive hyperemia. Ivy, Orndoff, Jacoby and Whitlow failed to observe any immediate, transient or permanent increase in the continuous secretion of saliva following small and large doses of roentgen rays. The excretion diminished after large doses, but this appeared to be a psychic inhibitory phenomenon, because the secretion returned to normal as soon as the dogs were put back into the stock.

In order to ascertain whether or not roentgen rays sensitize the submaxillary salivary gland to reflex or direct stimulation, from six to twelve control observations, extending over a period of from four to six weeks, were made on dogs with a Wharton duct fistula. The unirradiated glands were subsequently stimulated by the application of acid to the oral mucosa, by eating meat, and by the injection of pilocarpin. After a large number of preliminary observations had been made to establish the normal physiologic variations in the response of the gland to stimuli, the gland was irradiated and observations were made immediately afterward and again at intervals of from two to three days for a period of two weeks. Small doses did not cause any change in the secretion, either immediately or at any time afterward. Moderate and large doses also failed to produce any immediate effect on the secretion of saliva, but the secretion was diminished definitely one or two months after large doses of irradiation. Large doses likewise influenced the secretory response of the gland to reflex and direct stimulation; this response diminished within from ten to fourteen days following exposure, and the latent period also increased.

To ascertain whether or not a small dose of roentgen rays can stimulate a submaxillary salivary gland, the function of which has been depressed by any other means, 1.2 mg. of atropin sulphate was injected subcutaneously into one dog. After the secretory depression by reflex stimulation had been verified, the gland was irradiated at intervals of half an hour

[5] The first dose consisted of 50 peak kv.; 30 cm. focal distance; no filter; size of field, 6 cm. in diameter; 5 ma.; time of exposure, ten minutes. The second dose consisted of 100 peak kv., with the remaining factors unchanged. The third dose consisted of 145 peak kv., with the remaining factors as in the first dose.

for three hours after the injection and the secretory function was again tested at intervals of three days for two weeks following exposure. Three different doses of roentgen rays were used, but evidence of stimulation was not observed. No immediate change in the chemical composition of the saliva was found, but, within a month after irradiation, reduction in the viscosity and in the total solids of the saliva was observed, especially after stimulation by meat. The saliva became normal in composition after from two to three months, showing that the gland cells that are not destroyed by irradiation recover their full functional capacity and that the permanent reduction in the quantity of secretion is due to destruction of some of the gland cells.

Immediately following the experiments both the irradiated and unirradiated submaxillary glands were removed from each of the six dogs, fixed in Zenker and Bouin fluids, and stained with hematoxylin and eosin. Pathologic alterations were not observed in any of these glands, regardless of the dose of roentgen rays. The irradiated and unirradiated glands of four dogs were removed fifteen days and two months after the physiologic disturbance in function due to irradiation had occurred. The glands removed after an interval of fifteen days showed infiltration of round cells around the secretory ducts and blood vessels and also in the stroma of the gland, reduction in the amount of mucus stored in the alveolar cells and degeneration of some of these cells, and proliferation of fibroblasts in the stroma. The glands removed after a lapse of two months showed: diminution in size and increase in consistency, less round cell infiltration than after fifteen days, marked increase in the fibrous tissue of the stroma, and mucus distention of the alveolar cells. These pathologic changes correspond with the physiologic changes described previously.

In a previous series of experiments,[6] the results of which were briefly summarized, the authors stated they had been unable to demonstrate that small doses of roentgen rays stimulate or sensitize the submaxillary gland, but that large doses cause immediate depression of the secretory activity of the gland.

Case and Boldyreff (1925) carried out a series of experiments on three dogs[7], on each of which a salivary fistula (Pavlov) had been prepared surgically about one month previously.[8] Before irradiation a series of preliminary functional tests of salivary output were conducted to ascertain the quantity and quality of saliva secreted normally and after stimulation of the unconditioned reflexes by repeatedly introducing into the mouth of the dog a definite quantity of a definite stimulant such as 4.0 gr. of bread powder or 10 c.c. of a 0.4 per cent solution of hydrochloric acid, and the conditioned reflexes by exhibiting repeatedly to the dog some definite stimulant, such as bread powder or solution of hydrochloric acid. This was repeated at short intervals, the duration of stimulation was always thirty seconds, and the saliva secreted under such stimulation was collected, measured, and analyzed chemically for total solids, organic solids, and ash. The gland operated on was then exposed once to roentgen rays,[9] the remainder of the animal being thoroughly shielded from direct exposure. Physiologic observations were made twenty-four, forty-eight, and seventy-two hours, and one week after irradiation; subsequent observations were made at intervals of one week for some time, and later every two weeks.

In all three animals the secretion of saliva diminished greatly after irradiation, reached a minimum in three or four weeks, remained low for about a month, then slowly returned to normal. The secretory activity of the glands after irradiation was reduced to one-fourth or one-fifth in every animal. The composition of the saliva was affected, but the changes were

[6] The results of these experiments have apparently never been published.

[7] One male, weighing 26,000 gm.; one male, 18,000 gm.; one female, 20,000 gm.

[8] Two with fistula of the parotid gland; one with both a parotid fistula and a fistula of the combined orifice of the submaxillary and sublingual glands.

[9] The conditions of irradiation were: voltage, 200 peak kv.; distance, 50 cm.; filtration, 1 mm. of copper and 1 mm. of aluminium; 450 ma-min.

not constant. Case and Boldyreff concluded that this great decrease in salivary secretion was due partly to diminished sensibility of the buccal mucosa, but chiefly to a direct effect of irradiation on the glands themselves. They also suggested that the salivary glands should be examined microscopically to ascertain the effect of irradiation on their secretory and other cells during the period of minimum secretory activity. Such examination (Warthin) of the parotid gland of one of the dogs, which died from accidental cause after the termination of their experiments, did not reveal pathologic changes, and this was explained on the ground that the gland had long since recovered full functional activity.

Von Salis (1924) studied the effect of roentgen rays on the submaxillary and parotid salivary glands by applying to the corresponding region of each of two dogs large doses (eight to twelve times the usual dose given to man) of rays of unspecified quality, in several sessions at unstated intervals. The irradiated glands were removed after varying intervals and examined. The glands were removed from four unirradiated dogs for purposes of control. Swelling of the irradiated region appeared two or three days after exposure, and lasted from five to fourteen days. The salivary secretion remained unaltered.

Von Salis found, in almost all the cell groups in the irradiated glands, degenerative changes leading to destruction of the cells, interlobular infiltration of connective tissue, accumulation of mucus, clumping of cells and nuclei, and inflammatory edema. The excretory ducts were not affected, and the blood vessels were only hyperemic. The submaxillary glands were injured more quickly than the parotid glands, but both regenerated rapidly. The conclusion was drawn that the influence of roentgen rays is chiefly on the secretory function, which was said to be increased by "stimulating" doses and paralyzed by large doses.

Tsuzuki (1926) irradiated the entire body of rabbits with hard roentgen rays,[10] to test the effect of rays of short wave-length on the animals as a whole and on the different organs. Some of the animals were exposed, at one time, to doses varying between 20 and 100 per cent erythema dose, and were observed for a period of fifty-six days. Twenty-three rabbits were exposed once for from fifteen to one hundred twenty minutes (10 to 80 per cent erythema dose) and were killed at intervals of from fifteen minutes to ninety-six hours from the beginning of irradiation. Other rabbits were irradiated continuously until they died. All the animals that were not killed became emaciated gradually, often they suffered from diarrhea, and vital resistance was so weakened that they died from the slightest injury. Extensive cellular degeneration in the lymphatic system, spleen, bone marrow (leucocytes) and testis (spermatogonia) appeared soon after irradiation.

The salivary glands were not affected by doses smaller than 20 per cent of an erythema dose.[11] Doses of 30 and 40 per cent of an erythema dose caused only slight hyperemia within sixty minutes from the beginning of continuous irradiation. The hyperemia disappeared after forty-eight hours, and degeneration of the epithelium of the small ducts and irregular staining of the chromatin were noted. These alterations were not more accentuated forty-eight, seventy-two and ninety-six hours after sixty minutes of irradiation (40 per cent erythema dose). Directly after ninety minutes of irradiation (60 per cent erythema dose) hyperemia of the glands and epithelial degeneration of the small ducts and acini were apparent. Atrophy of the glandular cells was noted after intervals of twelve and thirty-six hours. The pathologic changes found after one hundred twenty minutes of irradiation (80 per cent erythema dose) were essentially the same, except that fatty degeneration of the epithelium lining the small ducts was present ninety-six hours after irradiation.

[10] The roentgen rays were gengrated by a Coolidge tube of the H-type supplied by a Neo-Intensiv-Reform-Apparat. Primary voltage: 220 volts; alternating 50 cycles; secondary voltage, 170 peak kv.; secondary current, 2 ma.; filter, 0.5 mm. copper and 1.0 mm. aluminium; parallel spark-gap, 25 cm. maximum; secondary voltage (measured by the minimum wave-length), 139 kv.; wave-length, 0.09 to 0.30 Angström unit averaging about 0.14 Angström unit; absorption coefficient, $\mu = 0.164$; depth dose calculated in the so-called "percentage depth dose" of Seitz and Wintz (10 cm. deep; focal-skin distance, 23 cm.; field 6 by 8 cm.) = 18 per cent; biological unit, as estimated by Seitz and Wintz = 50 minutes at 23 cm. focal-skin distance.

[11] This represents the dose to the skin of the back.

Radium. Horowitz (1911) irradiated organs of rabbits with 1 mg. of radium bromide in a thin-walled glass tube 1 cm. long and about 1 mm. in diameter. The tube was inserted into various organs, including the submaxillary salivary gland, and was left in place for ten days, unless the animal died. For purposes of control, the same tube, without radium, was introduced into the corresponding organs of other animals for the same length of time. The rabbits were then killed by dividing the medulla oblongata; portions of the irradiated and non-irradiated organs were fixed by various methods, imbedded in paraffin, and sectioned perpendicularly to the longitudinal axis of the canal formed by the tube. Other details, including the number and age of the animals, were not given. The salivary glands were said to have had a weak reaction to radium under these conditions, and yet destruction of the parenchyma and replacement by connective tissue were described.

Lazarus-Barlow (1922) exposed the entire body of twenty frogs, twenty-eight rats fifteen rabbits and nine cats to the gamma rays emitted by 5 gm. of hydrated radium bromide. The distance between the radium and the midpoint of the rats lying on the side was 4 cm.; the distance between the radium and the midpoint of the frogs, rabbits and cats exposed from above was 4 cm. for the frogs and 15 cm. for the rabbits and cats. The animals were usually killed by breaking the neck, either immediately after exposure or after varying periods, but some died during exposure. The tissues selected for examination were hardened for twenty-four hours in 10 per cent neutral solution of formol saline, washed in running water for several hours, passed through alcohol of gradually increasing strength, xylol, paraffin, and hematoxylin and eosin. Special preservation methods, such as the use of formol-Müller and osmic acid, and stains, such as Sudan, scarlet, Nile-blue, osmic acid and Pappenheim, were sometimes used.

Some of the frogs were exposed for three, six, or twenty-one hours and were killed immediately or three or four days afterward. Other frogs were exposed continuously for from forty-five to one hundred twenty-eight hours and all but two died spontaneously: three during irradiation, one shortly afterward, two two days, two five days, and one seven days after irradiation. Five rats were exposed for three hours; one for six hours, one for twelve hours, two for sixteen hours, one for twenty-four hours, one for forty-six hours and one for forty-eight hours. They were all killed immediately after exposure, except one which was found dead. Seven rats were irradiated for three hours; two were killed three days after exposure, one four days, two six days and two nine days afterward. Five rats were exposed for five and a half, twelve, sixteen, sixteen, and twenty-four hours, respectively, and they died or were killed thirty, two and a half, two, three, and two days, respectively, after irradiation.

Seven rabbits were exposed continuously for sixteen hours. Two were killed immediately, two three days, two six days, and one nine days after exposure. Two were irradiated for twenty-four hours and were killed nine days later. Two were exposed for sixteen hours and killed sixteen days later. Two were exposed for forty-eight hours; one died and the other was killed seven days later. One cat was irradiated for twenty-four hours and allowed to live. The seven other cats were exposed for twenty-four, thirty, thirty-six, forty-eight, sixty-four, ninety, and ninety-five hours, respectively, and died twelve, fourteen, six, five, eleven, two, and four days, respectively, after irradiation. One cat was exposed for ninety-six hours and died while under radium.

Definite pathologic changes were not observed in the serous salivary gland present in the rat, rabbit and cat. In the mucous salivary gland, however, mucoid change was marked, the cells were swollen, their outlines distinct, the nuclei contracted, deeply stained and pressed against the basement membrane. In the rabbit surviving seven days after a total exposure of forty-eight hours, edema and mucoid degeneration of the serous salivary gland was so great that this type of gland closely resembled the mucoid variety. The columnar cells lining the ducts were swollen and their nuclei intensely vesicular, while the lumen of the ducts contained granular, albuminous material, or was occluded by plugs of mucus.

Analysis of Experimental Data

Roentgen Rays. Ivy, Orndoff, Jacoby and Whitlow in experiments on the submaxillary salivary gland, demonstrated that small doses of roentgen rays have no apparent effect on the function of the gland, but that large doses of roentgen rays of medium quality cause a marked diminution in the secretion of saliva. This functional depression is not immediate, but appears from ten to fourteen days after irradiation, and continues for from one to two months. The experiments of Case and Boldyreff, who used a single large dose of roentgen rays of short wave-length, yielded results which agree closely with those of Ivy, Orndoff, Jacoby and Whitlow. The only discrepancy relates to the mechanism involved. Ivy and his coworkers attributed the depression in secretory activity to a vasoconstrictor action of the rays on the blood vessels, without giving the reasons for this assumption. Case and Boldyreff regarded it as a direct effect of irradiation on the salivary glands, which is to say on the secretory cells themselves. It is impossible to reconcile the interpretation of Ivy, Orndoff, Jacoby and Whitlow with the definite pathologic changes noted by them in glands removed fifteen days after the appearance of the physiologic disturbance in function induced by strong irradiation. These changes included degeneration of some of the epithelial cells lining the acini; reduction in the amount of mucus stored in the alveolar cells; lymphocytic infiltration around the secretory ducts and blood vessels and of the stroma itself, together with proliferation of the connective tissue in the stroma. The lymphocytic infiltration was less pronounced in the glands removed after a lapse of two months, but there was marked increase in fibrous connective tissue and the alveolar cells were distended with mucus. In the absence of other evidence these alterations must be regarded as a direct effect of irradiation on the gland, especially if the close accord between the physiologic and pathologic behavior of the gland is considered. The experiments of von Salis do not throw any light on the question, because his failure to give many essential details of technique makes it impossible to analyze his data. Moreover, evidence is not submitted to support the conclusion that stimulating doses increase salivary secretion. This conclusion is not supported by the other experiments on these glands.

Exposure of the entire body of animals (Tsuzuki) to roentgen rays of short wavelength also showed that the histologic structure of the salivary glands is not affected by small doses, that moderate doses cause hyperemia and degeneration, and that these changes are accentuated after large doses and are followed by destruction of the epithelium of the acini and ducts, fatty degeneration of the cells, and atrophy of the glands.

Radium. Direct exposure to the beta and gamma rays of radium by introducing into the substance of the glands thin glass tubes containing radium bromide (Horowitz) causes destruction of the glandular parenchyma and its replacement by connective tissue. This effect is largely, if not entirely, due to the intensely irritating action of the beta rays. Exposure of the entire body of animals to the gamma rays of radium (Lazarus-Barlow) shows essentially the same changes, though less pronounced, as those described by Tsuzuki, but the effect is chiefly on the mucous, rather than on the serous, salivary glands. Lazarus-Barlow (1922) applied radium (gamma rays) and Tsuzuki (1926) applied roentgen rays to the entire body of animals. The ensuing pathologic changes in the salivary glands are of the same degenerative character as those resulting from direct irradiation by Ivy, Orndoff,

Jacoby and Whitlow, by Case and Boldyreff, and by von Salis. But since it is possible that part of these alterations may have been secondary to the effect on the body as a whole, they cannot be regarded as undeniably, direct and specific.

The observation by Lazarus-Barlow of mucoid degeneration of epithelial cells, especially marked in the mucous salivary glands, indicates that the cells which secrete mucus are more radiosensitive than other epithelial cells. The significance of this fact appears all the greater when considered in relation to the parallel observation by Ivy, McCarthy and Orndoff, Mottram and others of mucoid degeneration in the mucus-producing cells of the intestine (q.v.) and when correlated with the well-known tendency of the salivary glands to react to irradiation. The foregoing experimental findings apparently furnish a logical explanation of the relative sensitiveness of the glands and of the clinical character of their reaction to irradiation.

Clinical Considerations

The exceptional sensitiveness of the salivary glands to irradiation has been known for many years. Bergonie and Speder (1911) recorded ten cases, four in which there was swelling of the parotid gland, four, swelling of the submaxillary gland, one, swelling of both the parotid and submaxillary glands and one, swelling of the parotid gland accompanied by dryness of the mouth. The swelling occurred a few hours after roentgen treatment for various conditions, and subsided spontaneously within from a few hours to a few days. Morin (1911) reported three cases of early reaction, without recognizing their true character. Ceresole (1912) presented what remains the best clinical description of the early phase of this phenomenon and reported twenty-one cases. Marques (1912) cited two interesting cases, and others, among whom may be mentioned Regaud (1912), Pfahler (1913), Schmidt (1914), Mühlmann (1919), Albert-Weil (1914), Jüngling (1923 and 1924), Christie (1924), von Salis (1924), Hirsch (1925), Solomon (1926), Pordes (1926), Heineke and Perthes (1925), have also called attention to the relative sensitiveness of the salivary glands to irradiation. With the exception of Ceresole, however, nearly all those who have mentioned the subject have done so only incidentally and have failed to distinguish the early from the late reactions and the influence of irradiation on the salivary glands from its action on the oral mucous membrane.

The unusual sensibility of the salivary glands may manifest itself by early reaction, by late reaction, or by combined reaction. The early reaction consists in rapid and often marked swelling of the glands irradiated, starting from three to six hours after exposure, reaching a maximum in from twelve to twenty hours, and subsiding spontaneously within from four to seventy-two hours. The swelling may be accompanied by slight pain and tenderness, but usually there is only a sensation of tension. This acute reaction occurs in a large percentage of cases in which the region of one or more of the salivary glands has been irradiated, but only in the glands that have been exposed in whole or in part to the direct action of the rays; the intensity of the reaction is proportional to the dose. Blondes are more susceptible than brunettes. According to Ceresole, the reaction develops in approximately 25 per cent of all cases in which therapeutic irradiation is carried out in the region of the salivary glands; 33 per cent of the patients were females and 19.6 per cent males. At present, some degree of reaction occurs in a large percentage of the patients irradiated; this is true of roentgen rays generated at both moderate and high voltage (rays of medium and

short wave-length). The parotid gland appears to be more sensitive than the submaxillary, but this is probably due to variation in the quantity of radiation reaching the glands; the parotid is nearer the surface, while the submaxillary lies deeper and is somewhat shielded by the inferior maxilla. The rapid onset and the distribution of the swelling lead many patients to think that mumps is developing; physicians are similarly deceived and are greatly puzzled by the rapid disappearance of the swelling and by the uniform absence of other symptoms that are usually associated with mumps. Moreover, the acute reaction leaves no trace of its passage in most cases, indeed in all cases uncomplicated by a late reaction.

The early, rapid and marked swelling of the glands after irradiation is probably caused by the accumulation and increase in specific gravity and viscosity of the saliva in the glands, the excretory ducts of which may be narrowed by cellular swelling or plugged with mucus. The function of the secretory cells is undoubtedly inhibited, but some time is required for this to become manifest. Strong irradiation should injure the vascular endothelium also, and this should tend to increase the inhibitory effect on the acinous epithelium. Meanwhile, the puzzling feature of the early reaction is the rapidity with which it subsides; this suggests a transient accumulation of saliva in the glands, but experimental and clinical evidence is too meager to provide an absolute explanation. The later phases of the reaction are distinctly due to the deficient secretory activity of the glands, plus the possible additional effect of strong irradiation on the mucous membrane of the mouth.

The late reaction is characterized by dryness of the mouth and interference with mastication and deglutition. It becomes perceptible from one to three weeks after exposure, and is caused by depression in the functional activity of the glands and the resulting diminution in salivary secretion induced by irradiation of all the salivary glands. The effect of irradiating the parotid and submaxillary glands on one side only is seldom sufficient to be noticed by the patients, because enough saliva is secreted by the unirradiated glands to moisten the mucous surfaces. The symptoms reach a maximum two to four weeks from the time of exposure and tend to subside slowly, but they may persist in some degree for several months. The severity and duration of the late reaction is also dependent on dosage. Both the early and the late reactions may be observed in certain cases, but the late reaction occurs only when all the salivary glands on both sides have been subjected to irradiation. Strong irradiation, especially with rays of short wave-length, may induce loss of sensation and dryness of the buccal mucosa and dryness and loss of taste of the lingual mucosa. This tends to intensify the dryness due to diminished salivary secretion. Cases such as that reported by Schmidt (1921) show that this effect of irradiation may occasionally be very rapid.

The cause-and-effect relationship between irradiation and these reactions is too obvious to admit of doubt, but the precise mechanism of both the early and late reactions is not so obvious. Probably they represent only different phases or stages of one and the same process. Heineke and Perthes (1926) have suggested that such reaction may be the indirect result of a direct action of the rays on the nerves supplying the blood vessels of the salivary glands. Mühlmann believes that irradiation acts on the glandular parenchyma itself or, in other words, on the acinous epithelium of the glands. If the great resistance of nerve tissue to irradiation is borne in mind, the

hypothesis of Heineke and Perthes does not appear to rest on a sound basis. It is possible that the endothelial cells lining the blood vessels are affected directly, because the sensitiveness of endothelium has been established, but the most important factor seems to consist in the exceptional susceptibility of the glandular epithelium itself, and especially of the mucous epithelium.

Although manifestations of the susceptibility of the salivary glands to irradiation are exceedingly common, it is surprising that they have received so little attention and study. The probable reason for this neglect is that the symptoms are seldom severe, that they abate spontaneously, and are overshadowed by the seriousness of most of the pathologic conditions for which roentgen or radium treatment is given to the regions occupied by the glands.

Parotitis. Acute parotitis is an uncommon but sinister complication of certain surgical operations. Its incidence is low in general surgery but higher in operations on the large intestine. The first record of the influence of irradiation on this disease appears to have been made by Heidenhain (1926), who found that the inflammation reacted to irradiation much as do many other acute inflammatory processes. Recently, Rankin and Palmer (1930) have found that the disease is from fifteen to twenty times more common after surgical intervention on the colon than after all other operations. The mortality rate as reported by various authors ranges between 35 and 60 per cent, and Rankin and Palmer stated that it depends on the primary condition, on the extent and severity of the operation, and on suppuration of one or both parotid glands. A moderate dose of radium applied soon after the onset of the parotitis (infiltrative stage) caused the inflammatory process to subside in most cases within from twenty-four to forty-eight hours and prevented suppuration; the mortality was correspondingly reduced. Suppuration was only a tenth as common after irradiation by radium as after ordinary methods of treatment. These conclusions were based on twenty cases, in only two of which surgical drainage had to be instituted. A few patients have also been treated with roentgen rays, with equally encouraging results. Radium is preferable in many cases of postoperative parotitis because the treatment can be given without disturbing the patient. Relief from pain and rapidity of regression are the salient effects of irradiation.

As in many other varieties of acute inflammation, the clinical circumstances following irradiation and a considerable body of experimental and histo-pathologic evidence suggest, as the best explanation for the therapeutic value of radiation, that the rays act chiefly by destroying the infiltrating lymphocytes. The fact that such destruction has not been found to cause any unfavorable effect may perhaps be accounted for by the liberation from the destroyed cells of the antibodies previously elaborated within them.

Von Mikulicz's Disease. Chronic, symmetric enlargement of the salivary and lacrimal glands known as "von Mikulicz's disease" is rare, and the pathogenesis is obscure. The swelling may begin in the lacrimal or in the salivary glands, but both groups of structures are generally affected. The disease may rarely be limited to the lacrimal or to the salivary glands, and cases presenting other atypical features have been described. The function of the glands may also be interfered with. Systemic reaction, if any, is only slight. The lymphatic system, and the liver and spleen remain normal; the corpuscular elements of the blood are unaltered. According to von

Mikulicz, who first described the condition, its pathologic characteristics are essentially chronic inflammation and marked round cell infiltration of the glands. Aschoff regards it as an unusual manifestation of Hodgkin's disease.

Fittig (1904) apparently was the first to use roentgen irradiation in the treatment of von Mikulicz's disease. Haenisch (1906), Pfeiffer (1906), and Ranzi (1906) also reported, at about the same time, cases treated in this manner, in which great benefit or cure was derived. Since then other cases have been reported by Lacour and Barjon (1909), Saussol (1910), Séjournet (1910), Chuiton and Aubineau (1912), Duranti (1913), Rieder (1922) and Jackson (1925). It is doubtful if cases, such as those reported by Jacobaeus (1909), Lüdin (1916), Hörhammer (1918), Gaisböck (1918), Reiche (1919), Cogolli (1921), Ziegler (1926), and others, are true examples of the disease described by von Mikulicz; they probably represent unusual manifestations of lymphoblastoma. However, a clear distinction between von Mikulicz's disease and lymphoblastoma has not yet been made.

Pfeiffer described two cases, only one of which was characteristic of von Mikulicz's disease. Microscopic examination of a section of one of the enlarged submaxillary glands removed before irradiation showed marked infiltration of round cells, partly diffuse and partly circumscribed, with numerous conglomerate, or giant, cells. The lymphocytic infiltration was most pronounced between the acini toward the periphery of the gland and around the larger excretory ducts. In certain parts of the section, especially near the center of the gland, the acinous structure had been replaced by connective tissue, and round cells were almost entirely absent from such areas. The lymphocytic infiltration had disappeared almost entirely from sections of one of the submaxillary glands removed after irradiation; there was less crowding together of the acini and still greater proliferation of connective tissue, but no change in the acinous epithelium. In an effort to explain the mode of action of irradiation, Pfeiffer also examined sections of a lymph node removed from the same patient before irradiation and of another node removed after irradiation. He found that the changes induced by repeated exposure to roentgen rays were precisely similar and also consisted chiefly in marked destruction of lymphocytes and proliferation of connective tissue. This is an interesting and valuable observation, because it tends to confirm the idea that von Mikulicz's disease is essentially lymphoblastomatous, and because the changes noted after irradiation correspond with those induced in normal lymphatic structures and in the various manifestations of lymphoblastoma.

Salivary Fistula. Advantage has been taken of the sensitiveness of the salivary glands to irradiation to control, by means of roentgen rays, the outpouring of saliva which so often interferes with the healing of traumatic fistulas of the glands. Such fistulas, usually of the parotid gland, are often the result of gunshot or duelling injuries, and many radiologists, chiefly German, have reported the successful use of irradiation during and since the war. Thus, Fraenkel (1916), Holfelder (1922), Kaess (1923), Schaedel (1923), Kleinschmidt (1923), Henke (1924), Kremer (1925), Rahm (1927), and others have recorded cases in which the flow of secretion from salivary fistulas had made attempts at surgical repair unsuccessful. After roentgen irradiation in these cases the fistula closed spontaneously, or surgical repair was effectively performed.

Excessive Secretion of Saliva. Irradiation has also been used to check the excessive secretion of saliva associated with certain lesions. FRAENKEL (1923) employed roentgen rays for this purpose in a case of chronic, lethargic encephalitis, with increased salivary secretion, and the flow of saliva returned to normal. BIERMER (1924) reported similar success in a case of ptyalismus gravidarum.

Conclusions

The few animal experiments conducted with the object of determining the action of irradiation on the mucous membrane of the mouth indicate that strong doses of roentgen rays, especially rays of short wave-length (doses sufficient to cause erythema in the skin of the cheeks), may diminish the sensibility of the oral mucosa, which generally recovers. The duration of this effect varies according to the quantity and quality of the rays; the recovery of the mucosa, therefore, may be rapid or slow, complete or incomplete.

There is no valid evidence that small doses of radiation increase the functional activity of the salivary glands; on the contrary, the evidence indicates that small doses have no effect, but that strong doses interfere with their function and diminish the secretion of saliva by causing metabolic inhibition and degeneration of the specific epithelium of the glands. The degree of such action, as well as its onset and duration, depend on the dosage, and the effect of irradiation may be temporary or permanent for the same reason.

The salivary glands are exceptionally sensitive to irradiation. The reaction of the glands thus induced may be early, late, or combined. Early reaction occurs in a large percentage of cases in which the region of one or more of the glands is irradiated, and consists of rapid swelling, with a sensation of heat and tension. The swelling begins a few hours after irradiation and generally subsides spontaneously within from twenty-four to seventy-two hours. Females are twice as susceptible as males, and blondes more susceptible than brunettes. The late reaction consists in dryness of the mouth which appears from a few days to two or three weeks after irradiation of most or all of the salivary glands, is most pronounced two to four weeks after exposure, subsides slowly thereafter, and is due to decreased secretion of saliva. Its severity and duration vary with the dosage. Both the early and late reactions may occur in the same case.

Irradiation has proved definitely useful in the treatment of acute parotitis and von Mikulicz's disease, probably because of the great influence on the lymphocytic infiltration or proliferation which characterizes these conditions; of parotid fistula from trauma, and of the excessive secretion of saliva occasionally associated with pathologic disturbances, such as lethargic encephalitis and pregnancy.

ESOPHAGUS

The situation of the esophagus undoubtedly affords exceptional protection from injury by irradiation, but, aside from this, the specific radiosensitiveness is not great. Few injuries of this structure have been recorded and consequently its sensitiveness has not been subjected to experimental investigation. Nevertheless, injury by irradiation of the esophagus may occur, as is shown by a case reported by Rahm (1927). Injury probably can occur under concentrated exposure to irradiation of short wave-length or to radium introduced into the lumen of the esophagus.

STOMACH

General Considerations

Exposure of the stomach to roentgen rays is commonly followed by clinical manifestations, such as anorexia, nausea and vomiting, but since similar manifestations accompany irradiation of other regions the relationship between them and the direct action of the rays is still a matter of conjecture. These clinical disturbances will be reviewed elsewhere. The experimental and clinical data with regard to the specific sensitiveness of the stomach to roentgen and radium rays have often been interpreted with considerable freedom, but they are far from complete. It will be interesting, therefore, to review this evidence and to see what conclusions may fairly be drawn from it.

Animal Experiments

Roentgen Rays. REGAUD, NOGIER and LACASSAGNE (1912) irradiated[12] the abdomen of six healthy female dogs. Necropsy was performed on all of the dogs and the stomach and intestine of four were examined microscopically.

The first dog, weighing 13 kg., was about three weeks pregnant and received over a large portion of the intestine 10 Holzknecht units of rather soft roentgen rays[13] in one hour. Diarrhea supervened immediately and the dog died in less than thirty-six hours. The uterus was in full abortion, without hemorrhage but with intense congestion. It contained five embryos measuring from 12 to 13 mm. and separated from the mucosa. There was slight diffuse hemorrhage in the digestive tract, but no peritonitis. The intestinal mucosa was red and covered with an abundance of thick, adherent, chocolate-colored mucus.

The second dog, weighing 15.5 kg., was irradiated over the posterior (pelvic) half of the abdomen and received 5 Holzknecht units of soft roentgen rays[14] in one hour and twenty-five minutes. The animal soon began to lose appetite and weight and died twenty-two days later. Eighteen hours after death the peritoneum was reddish, but free from exudate, and there was no sign of perforation. Because the dog had eaten chicken bones two days before death and anorexia began shortly after this, death was believed to be due to intestinal infection, made possible by a lowered resistance of the intestinal mucosa resulting from irradiation.

The third dog, weighing about 6 kg., received an injection of 0.03 cg. of morphine and approximately 9 Holzknecht units of soft roentgen rays[15] in one hour and ten minutes. This was directed to the region of the stomach, the greater part of the intestine being excluded. The animal did not eat for three days after exposure and its weight fell 250 gm. in ten days. Two weeks after the first exposure the gastric region was again exposed to 9 Holzknecht units under the same conditions as for the first irradiation. Complete anorexia ensued for two days and partial anorexia for a third day. The weight of the animal fell 500 gm. during the next nineteen days, when a third similar dose of roentgen radiation was given to the gastric region. During the next eight months the weight of the animal decreased 500 gm. The entire abdomen was then given 14 Holzknecht units of roentgen rays[16] in two hours. This was again followed by anorexia for two days. One hundred and fourteen days later the weight of the dog was 4 kg., but its appetite was good and its condition otherwise satisfactory. The entire abdomen was again irradiated, 22 Holzknecht units[17] being given in one hour. The dog soon

[12] Muller "rapid" type tube, with water-cooled anticathode. A description of the generating apparatus was not given. The dose was measured by means of pastilles of barium platino-cyanide. The color changes were determined in broad daylight according to the chromoradiometric scale of Bordier and converted into Holzknecht units.

[13] Focal-skin distance: 25 cm.; filtration: 2 mm. aluminium. The dose at the level of the skin was estimated as 11½ on the Bordier scale.

[14] Filtered through 2 mm. of aluminium, at a focal-skin distance of 31 cm.

[15] Filtered through 2 mm. of aluminium, at a focal-skin distance of 31 cm.

[16] Filtered through 3 mm. of aluminium, at a focal-skin distance of 28.5 cm.

[17] Filtered through 4 mm. of aluminium, at a focal-skin distance of 19 cm.

became very ill, stopped eating, and bloody diarrhea developed; it grew weaker and succumbed twenty-eight days after the fifth exposure. An extraordinary number of Taenia was found in the intestine, which did not contain feces or food particles. The peritoneum was normal. On microscopic examination the midgastric region showed marked atrophy of the glands; this atrophy involved particularly the chief cells and was held responsible for the progressive cachexia.

The fourth dog, weighing 8.75 kg., received over the upper abdomen, including the stomach and part of the intestine, 20 Holzknecht units of soft roentgen rays[18] in sixty-five minutes. This was followed by anorexia, bloody diarrhea and progressive emaciation; death ensued eighty-one days after irradiation. Necropsy revealed perforation with seropurulent peritonitis at the juncture of the anterior two-thirds and posterior third of the small intestine. The small bowel was filled with thick, adherent, mucopurulent material; the large intestine did not contain pus. The glands of the pyloric region were normal, but those of the fundus were definitely atrophied. The chief cells appeared shrunken and some of the border cells were vacuolated. The epithelium of a portion of the small intestine was desquamated. In some segments the glands of Lieberkühn were partly atrophied, and their epithelium was flattened. In other segments marked atrophy of the glands was noted, but glands were completely absent from the region surrounding the perforation. Everywhere the interglandular connective tissue showed extensive leucocytic infiltration, which extended into the muscularis.

The fifth dog, weighing 13.75 kg., received 20 Holzknecht units of soft roentgen rays[19] over the upper part of the abdomen in one hour. Anorexia, vomiting, bloody diarrhea, and progressive emaciation for six weeks followed. The animal then recovered slightly, but remained cachectic and was killed at the end of three and a half months. The stomach appeared normal at necropsy, but microscopic examination showed slight atrophy of the glands, involving especially the chief cells. In the mucosa of the small intestine, near the juncture of the anterior two-thirds and the posterior third, was a rounded ulcer 8 to 10 mm. in diameter, undergoing cicatrization; this was surrounded by a zone of thickening and induration. The small bowel contained a large number of Taenia. There was also slight atrophy of the intestinal glands of Lieberkühn and an increase of the interglandular connective tissue, with many migrating cells. The glandular atrophy was particularly marked in the vicinity of the perforation.

The sixth dog, weighing 17 kg., was irradiated[20] twice within fifteen hours over a large portion of the abdomen, three weeks after having given birth to three pups. Forty hours after the first exposure the animal refused food and was killed at the end of the third day. The stomach contained about 50 c.c. of mucous liquid, and its inner surface was pale but otherwise normal. Microscopic examination did not reveal topographic disturbance of the glands, but the chief cells were shrunken and partially desquamated. About half of the parietal cells were swollen, vacuolated and free from granules. There was abundant evidence of diapedesis. The intestine contained only sticky mucus and many Taenia. The intestinal epithelium was flatter than normal and often separated from the stroma of the villi by abundant leucocytic infiltration and by masses of delicate interlacing filaments, probably fibrin. These changes were greatest in the loop of bowel in contact with the abdominal wall. The glands of Lieberkühn showed flattening of the epithelium, shrinking and indistinctness of cells, and swelling of nuclei and fragmentation of the tubules, some of which had completely lost their epithelium. There was also increase of connective tissue, leucocytic infiltration, and dilatation of the capillaries. The subglandular layer of lymphoid cells was indistinct, and the injured cells were scattered between the glands.

[18] Filtered through 4 mm. of aluminium, at a focal-skin distance of 18.3 cm.

[19] Filtered through 4 mm. of aluminium, at a focal-skin distance of 18 cm.

[20] Filter, 0.92 mm. of aluminium; focal-skin distance, 22 cm.; duration of exposure, 65 and 88 minutes respectively; total dose for the two sessions, 70 to 75 Holzknecht units.

From these results Regaud, Nogier and Lacassagne concluded that the superficial epithelium of the gastric mucosa is not particularly sensitive to radiation, but that the epithelium of the fundus is more sensitive than that of the pyloric region; that irradiation may produce acute or chronic lesions according to the dose and the length of survival or observation; that the lesions in the intestine induced by irradiation involve chiefly the villi, the glands of Lieberkühn and the lymphoid and connective tissues of the small bowel; that the epithelium first becomes detached from the villi, and the stroma shrunken; that the villi finally disappear, and that the glands of Lieberkühn appear most sensitive and can be made to disappear in a few days.

Ghilarducci (1914 and 1916) investigated the action of roentgen rays on the stomach of thirty-four rabbits, with and without preliminary ingestion of bismuth, on the assumption that the presence of this heavy metal in the stomach during irradiation would probably cause the generation of large quantities of secondary rays. Seventeen of the animals were exposed[21] after bismuth ingestion, and seventeen others without bismuth. Sections from the stomach of each animal were fixed in formaldehyde or Müller's fluid, with acetic acid added; they were imbedded in paraffin and stained with hematoxylin and eosin or with orange.

Ulcerative or necrotic lesions in the mucosa of the stomach, plainly visible with the naked eye, were found in twenty-nine of the thirty-four animals. Perforating ulcers were observed in three instances. Such lesions occurred in all the rabbits exposed after the ingestion of bismuth and in twelve irradiated without bismuth. As may be surmised, the weight of the animals was an important factor by its influence on the depth dose. Thus nine rabbits weighing from 850 to 1,300 gm., irradiated after the ingestion of bismuth, showed gastric lesions and eight control animals of the same weight also showed lesions. On the other hand, nine rabbits weighing from 1,800 to 2,000 gm., irradiated after the ingestion of bismuth, yielded but four positive results, and only three of the five control animals of corresponding weight showed gastric lesions. Gastric abnormality was found in all four rabbits weighing from 2,100 to 2,500 gm. irradiated after the administration of bismuth, but in only one of the four animals irradiated without bismuth.

Necrosis of glandular tubules and areas of great destruction of the mucosa, down to and sometimes affecting the muscular layer, were found. In three instances the muscularis was destroyed, and the base of the ulcer consisted of newly formed connective tissue. With necrosis of the mucosa there were often scattered hemorrhages, especially in the smaller animals. Moderate atrophy of the mucosa was almost constantly noted, especially in the rabbits irradiated after the ingestion of bismuth. This atrophy affected particularly the chief cells, but sometimes it affected the entire epithelium, and was present even when necrosis was absent. Many of the chief cells had undergone degeneration and disappeared. The parietal cells had suffered less. Leucocytic infiltration also was common. Ghilarducci regarded these changes in the gastric mucosa as due primarily to the direct effect of the rays on the epithelium of the gastric glands. He also postulated a possible stimulating action of irradiation, but his experiments do not furnish evidence of such action.

Szegö and Rother (1921) reported at length their experiments on the effect of roentgen rays on the functional activity of the stomach of one dog. A gastric fistula was made in the deepest portion of the fundus, and the condition was verified by repeated roentgenologic examination, which also served to reveal the exact position of the stomach. Esophagotomy was performed fifty-five days later. The general condition of the animal deteriorated for a time, but it lost only 1.1 kg. in weight. An ulcer on the right forepaw developed from the constant dripping of gastric secretion, and other exudative or scaly lesions appeared on the

[21] The quality of the rays varied between 10 and 14 Wehnelt; the quantity, between 10 and 30 x units (Kienböck); the intensity, between 2 and 3 ma.; the duration of exposure, between five and twenty minutes; the filter, between 1 and 4 mm. (probably aluminium); the weight of the animals, between 850 and 2,500 gm.The tube was operated in connection with an induction coil of 30 cm. spark-gap, with large model, Ropiquet interrupter (the interruptions varied between 4,000 and 8,000).

face and neck, but these all healed within a month with the use of silver nitrate and balsam peru, and the body weight returned to normal. The possible mixture of bile and gastric juice was avoided by using only secretion free from bile. Cicatricial contraction of the esophageal fistula was counteracted by manual dilatation. The nutrition and health of the dog was maintained at an approximately constant level by careful preliminary feeding tests and by uniformity in the experimental conditions. The animal, which was kept by itself and with all disturbing factors excluded, was given each morning, through the gastric fistula, 100 gm. of boiled meat, 250 gm. of ground bone, and 400 gm. of mashed potato. Each evening the cannula closing the gastric fistula was removed and the stomach washed and thoroughly evacuated through a tube introduced into the esophagus. Then three-fourths of a liter of water was given through a stomach tube passed into the esophageal fistula. The following morning, before the sham feeding and after the dog had been weighed and tamponed, a half pound of raw horse meat, cut into small pieces, was given piece by piece for twenty minutes. The dog was then secured firmly. The first drop of gastric juice appeared regularly five minutes after the feeding. The secretion was collected and divided into four portions: the first portion taken fifteen minutes after the flow started (twenty minutes after the beginning of the sham feeding) and the three other portions at intervals of one hour. The meat used for the feeding was then mixed with 100 gm. of bone meal and 400 gm. of potato flour and given the animal through the fistula.

The gastric secretion, usually clear and colorless, was at times opalescent and rarely had a faint yellow tinge from the slight admixture of bile. The total acidity and free hydrochloric acid were generally determined with a fiftieth normal solution of sodium hydroxide, using dimethylamidoazobenzol and phenolphthalein as indicators. From the quantity of secretion and from the titration values for each sham feeding the amount of free and combined hydrochloric acid in milligrams was ascertained. The total chlorides were determined by the Volhard method.[22] Rennin was estimated chiefly by the method of Michaelis, and pepsin by the Fuls-Edestin and the sulphosalicylic acid precipitation method of Michaelis. Controls were used throughout for these estimations. The experimental conditions were carefully checked over a preliminary period of two months. The dog was then irradiated,[23] the beam of rays being directed upward so as to include with certainty the fundic portion of the stomach, and the sham feeding, and the acid, pepsin and rennin estimations were repeated daily as before. The dog was irradiated a second time[24] seventeen days, a third time forty-seven days, a fourth time sixty-one days, and a fifth time[25] sixty-nine days, respectively, after the first irradiation.

The acidity and the chloride and pepsin values of the gastric secretion did not vary from normal after the first two exposures to roentgen rays within the range of therapeutic dosage for man. The rennin showed no variation for twenty-seven days (nine sham feedings) after the first, and for ten days after the second irradiation; it then diminished slightly, but soon rose again and finally increased above the normal level. The dose of roentgen rays given at the third and fourth exposures was much stronger than that used for the first and second exposures and represented two or three times the limit of therapeutic dosage for man. Before each of these two irradiations the stomach was filled with barium meal "to produce second-

[22] Always between 0.49 and 0.56 gm. for each 100 c.c. of gastric juice.

[23] Technique of first irradiation: Symmetrie apparatus; self-hardening boiling water tube, with automatic regeneration; filtration of 0.5 mm. zinc and 1.0 mm. aluminium; focal-skin distance, 23 cm.; size of field, 10 by 14 cm.; secondary voltage, 100 kv.; secondary current, 2 ma.; 38 per cent of erythema skin dose at a depth of 3 cm. in 100 minutes.

[24] Technique of second, third and fourth irradiations: Veifa-Reform apparatus; Coolidge tube; filtration of 0.2 mm. copper and 3.0 mm. aluminium; focal-skin distance, 24 cm.; size of field, 6 cm. in diameter; parallel spark-gap, 21 cm.; secondary current 2.5 ma.; second irradiation, 47 per cent erythema skin dose, at a depth of 3 cm. in 48 minutes; third irradiation, 88 per cent erythema skin dose, at a depth of 3 cm. in 90 minutes; fourth irradiation, 116 per cent erythema skin dose, at a depth of 3 cm. in 120 minutes.

[25] Technique of fifth irradiation, same as that of second, third and fourth, except that a filter was not used; duration of exposure, 90 minutes. Dose many times those previously given.

ary rays." These third and fourth exposures were said to have been followed by an increase in the quantity of gastric secretion and a rise in the total and free hydrochloric acids, the pepsin and rennin. Szegö and Rother interpreted this as a manifestation of gastric stimulation by the rays. The increase was short-lived and the next sham feeding was followed by a proportional decrease below the previously normal level; this decrease in the quantity of secretion, in the total acidity and free hydrochloric acid, and in the pepsin and rennin values was regarded as evidence of injury to the gastric glands. The same effect of greater variation above and below the previous normal range of variation was observed after both the third and fourth irradiations (strong doses), but the gastric juice rapidly returned to normal.

Szegö and Rother concluded that small doses of roentgen rays have no effect on the gastric secretion, but that very large doses cause transient increase, followed by a more lasting decrease, in the quantity of juice secreted, in the total acidity and free hydrochloric acid, and also in the pepsin and rennin. However, gastric secretory function always returned to normal later.

The fifth irradiation, given sixty-nine days after the first, consisted of a dose of unfiltered roentgen rays "scarcely compatible with life." The dog rapidly became dejected and vomited all day through the esophageal fistula. There was bloody diarrhea and gradual emaciation. A second degree radiodermatitis appeared in the irradiated area. Ninety-nine cubic centimeters of bile-colored gastric juice was collected in forty-five minutes; its total acidity was low and it did not contain free hydrochloric acid. The dog was killed by injecting chloroform into the heart. At necropsy the external field of irradiation was found to correspond with the greatest portion of the anterior and posterior walls of the stomach. The mucosa of the irradiated portion of the organ showed marked atrophy and numerous petechiae. The mucosa of the irradiated portion of the stomach was less than half as thick as that of the unirradiated portion, and this thinning of the mucosa affected the lamina propria, and the muscular and submucous coats. Except for scattered rests, the epithelium of the excretory spaces had disappeared. Marked proliferation of the connective tissue was seen in the deep portion of the mucosa, giving it a sclerosed appearance. The acinous epithelium was atrophic and some of it had become cystic. Neither mother nor delomorphic cells could be found in this epithelium, and lymphocytic infiltration was not present. The mucosa of several portions of the small intestine was absent, and there were extensive hemorrhages, but no changes in the serosa. The epithelium of such portions had disappeared completely; there was an accumulation of round cells on the denuded surface, and moderate proliferation of the connective tissue extended from the muscularis mucosae.

Ivy, Orndoff, Jacoby and Whitlow (1923) investigated the effect of roentgen irradiation on the stomach of six dogs, on each on which a Pavlov pouch had been prepared. Two or more weeks after the surgical construction of this pouch, preliminary control determinations of the continuous secretion of gastric juice by the pouch were made for one or two hours. A test meal was then given to each animal and the gastric secretion collected hourly for four hours after the meal.[26] Each hourly quantum of secretion was measured, titrated for free and total acidity, examined for peptic activity by the Mett tube method and analyzed for concentration of chlorides. After from ten to twenty such control determinations had been made to ascertain the normal physiologic variation in gastric secretion, the Pavlov pouch of each animal except one was exposed to a different dose of roentgen radiation.[27] The beam of rays was directed so as to strike only the pouch and the overlying abdominal wall. It was impossible to exclude the spleen, but the intestine was excluded. A test meal was given after each

[26] The test meal consisted of 250 gm. of ground raw meat.

[27] The smallest dose employed was given as 60 kv.; 3 ma.; focal-skin distance, 30 cm.; size of field, 6 cm. in diameter; no filter; time, 3 minutes (approximately 30 per cent of a human erythema dose, and 10 per cent of a dog erythema dose). The largest dose is given as: 110 kv.; 5 ma.; focal-skin distance, 30 cm.; filter, 1 mm. aluminium; size of field, 6 cm. in diameter; time, one hour (approximately 165 per cent of a dog erythema dose, and over 400 per cent of a human erythema dose).

irradiation and the secretion was collected, measured and tested every other day for from three weeks to three months, before the animals were again irradiated.

The normal variation in the interdigestive secretion of gastric juice was from 0.5 to 2.0 c.c. each hour, and in the total acidity, from 0.02 to 0.10 per cent. The authors were unable to find a dose of roentgen rays which increased the amount or the acidity of the gastric secretion, but a large dose [28] abolished the secretion, and only mucus was secreted by the gastric mucosa ten to fourteen days after irradiation. Free acid was absent from the secretion for a period of three weeks, but the acidity returned to normal after six weeks, although the quantity of gastric juice remained 50 per cent below the normal. The secretion of pepsin also decreased after large doses of roentgen rays, but not to the same extent as the secretion of acid. The chloride content of the secretion was not appreciably altered. Only half of the Pavlov pouch of one dog was irradiated, and the production of acid and pepsin ceased in the irradiated portion; the unirradiated half of the pouch continued to produce acid. One dog died from acute roentgen "cachexia"; some of the others were killed from ten to fourteen days after irradiation. Petechiae and small ecchymotic hemorrhages were found in the mucosa of the Pavlov pouch of each of these animals.

Ivy and his coworkers interpreted these results as due chiefly to the effect of irradiation of the gastric mucosa itself, but they believed that a general systemic effect may also have played a part in the depression of gastric secretion by large doses of roentgen rays. They added that the gastric glands of the dog are 40 per cent more sensitive to irradiation than the salivary gland and less sensitive than the small intestine.

The pathologic changes in the Pavlov pouch of the dogs were described by Dawson (1925), who stated that the changes produced by a single large dose and by repeated smaller doses were identical. Fresh tissue from the pouch of each dog was fixed in formol-Zenker solution, and serial sections were stained with hematoxylin and eosin, iron hematoxylin, neutral gentian, mucihematein, and polychrome methylene blue. The mucosa from the pouch of dogs that had received less than 155 per cent of a dog erythema dose, or three and one-half times a human erythema dose, was normal, but the mucosa from the pouch of dogs that had received this or still larger doses showed definite pathologic changes. These were characterized by destruction of some of the epithelial cells, the mucous and neck cells being especially prone to injury, but the chief and parietal cells also may be injured. The chief cells in the superficial third of the mucosa had undergone cytolysis and the pepsin granules had been set free in the lumen of the injured glands. The parietal cells were more resistant. Some of the apparently intact chief cells were functionally inert, because free acid could not be detected in an irradiated pouch. Although petechial hemorrhages and hyperemia were present in the mucosa, it was impossible to determine whether the blood vessels or the gastric epithelium were affected primarily, or whether both were injured simultaneously. Infiltration of leucocytes was not noted in any case. The fibroblasts showed some hypertrophy but no proliferation. All the pouches which subsequently recovered normal function were found histologically complete, but the mucosa of the regenerated pouches was only about half normal thickness. Phagocytosis was not observed, and there was little fibrosis in the repaired mucosa. The parietal cells showed great variation in staining and in nuclear structure; some were pale, with a pycnotic nucleus, while others stained densely and their nucleus showed a definite reticulum.

Miescher (1923) tested the effect of roentgen rays on the gastric secretion of a dog one and a half years old, weighing 22 kg. The first step was the surgical preparation of a Pavlov pouch, after which the animal was used for various physiologic experiments for some time. The dog was fed on a standard mixture consisting of 650 gm. of mixed chopped meat, water and bread. The proportion of these items was not specified but was always the same. The

[28] One and two-third times the erythema dose for the dog.

animal was kept in the same surroundings, and psychic disturbances were avoided by regular habits. The gastric secretion from the Pavlov pouch was collected by means of a tube which conducted the secretion to small paraffined glasses used for measurement and titration; these glasses were changed at intervals of a fourth to a half hour until the secretion stopped from three and a half to four and a half hours later. The secretion was always clear, faintly yellow, and contained small flecks of mucus which were removed with a fine hook. The total acidity and free hydrochloric acid were determined by titration with a twentieth normal solution of sodium hydroxide, and methyl orange and phenolphthalein were used as indicators. The concentration of pepsin was ascertained by the method of Mett and by following strictly the recommendations of Nierenstein and Schiff. Determinations were made daily, at intervals of from two to four days or, sometimes, at still longer intervals; the experiment was continued throughout a year.

The entire region of the stomach, verified by roentgenologic examination, was exposed from the right and left sides to two preliminary irradiations[29] (small dose) in order to accustom the dog to such exposure. Two days after the last preparatory exposure (May 1, 1920) the region was irradiated through the left side with a dose of 1.0 Sabouraud, measured in the stomach, and the effect was followed closely during the next eight months. December 17, the region was irradiated from both sides, each side receiving 1.6 Sabouraud.[30] The same dose was repeated January 7 and 28, and February 19, 1921, each side being given 2.0 Sabouraud doses.[31]

During the first few days after each irradiation the dog was restless, nauseated and without appetite; several times food was vomited immediately and was immediately re-ingested. Diarrhea occurred on three occasions, but was never blood stained. As a rule these symptoms disappeared from two to seven days after irradiation. The two first preparatory irradiations were followed by slight variations in the quantity and acidity of the secretion; these were attributed to psychic factors. Three days after the first strong irradiation (May 1, 1920) the quantity of gastric secretion increased about 18 per cent and, except for a transient drop on the eighth day, the secretion increased for almost fourteen days. The daily output of gastric juice then decreased to normal and below, but the quantity of secretion then increased progressively for several months and remained permanently at a higher level than before irradiation. Gastric acidity decreased considerably soon after irradiation and then slowly returned to the pre-irradiation level or slightly above.

Two days after the strong irradiation given December 17, 1920, the quantity of secretion increased slightly, dropped on the fourth and fifth days, jumped to 130 per cent of the pre-irradiation level, then fell below the initial level, and irregular oscillations below the normal level continued for several days. After each subsequent exposure to a strong dose of roentgen rays there was a sharp increase in the quantity of secretion, followed by a drop below the initial level, and this in turn was succeeded by irregular oscillations, with a gradual tendency to rise. Throughout the period of these repeated irradiations the secretory activity was below the normal level, but it returned to normal one and a half months after the last irradiation.

The acidity fell sharply after each irradiation, and this drop was not preceded by any rise in the curve. The acidity then remained low for several days and gradually rose. After the irradiations were stopped acidity returned to normal more rapidly than the daily output of

[29] The roentgen rays were measured by the photographic method of Kienböck. The strips of photographic paper, protected by a rubber finger cot, were introduced into the Pavlov gastric pouch, and the dosage estimations made by means of these strips were checked against Sabouraud pastilles. Irradiation was carried out with a self-hardening, boiling-water tube, operated in connection with a Symmetrie apparatus at a voltage equivalent to a parallel spark-gap of from 33 to 35 cm. between points. The current intensity was 2.2 ma.; the filtration 4 mm. of aluminium; the focal-skin distance, 30 cm.; and the size of the fields 15 by 20 cm. With the tube used under these conditions a full Sabouraud dose was stated to correspond to about one-third of an erythema skin dose.

[30] Total dose in the stomach given as 2.25 Sabouraud.

[31] Total dose in the stomach given as 2.8 Sabouraud.

secretion. The pepsin was but slightly influenced by the early irradiations, and it reacted slowly to subsequent exposures, but the reaction was always downward. After the third strong exposure the pepsin value remained little above zero until the irradiations were discontinued, when it gradually mounted toward the normal level. This regeneration was more sluggish than both the secretory output and the acidity.

Miescher warned against the conclusion that the rise in gastric secretion immediately following irradiation should be regarded offhand as a result of direct stimulation by the rays. Also that the depressor effect on gastric acidity cannot be maintained indefinitely, because the stomach seems to acquire a certain tolerance to irradiation. He made the interesting observation that a traumatic ulcer, which had formed at the point of union between the gastric fistula and the skin and which had increased steadily in size, healed after two irradiations had depressed gastric acidity to a low level.

Tsukamoto (1924) irradiated the hepatic region of many rabbits in order to ascertain the effect of roentgen rays on the liver and on general metabolism. The irradiation was carried out through two opposite fields, and the dose varied between 100 and 400 per cent at the surface, or between 135.4 and 541.6 per cent at a point midway between the two surfaces.

One rabbit was exposed four times[32] at intervals of one or two weeks for thirty, forty, fifty, and sixty minutes, respectively, and was killed eighteen days after the last irradiation. One animal was exposed four times at intervals of from two to sixteen days for forty, fifty, sixty, and ninety minutes, respectively, and died one day after the last exposure. One rabbit was irradiated[33] twice at intervals of nine days for ninety minutes and died eleven days after the second exposure. The hepatic region of two rabbits was irradiated[34] once through each of the two fields for one hundred twenty minutes, and the animals were killed thirteen and eighteen days later, respectively. In one rabbit, each of two opposite fields corresponding to the region of the liver was exposed to roentgen rays[34] for 160 minutes, and the animal died nine days later. One rabbit was irradiated[35] through each of two hepatic fields for forty minutes twice with an interval of four days, and died seven days after the second exposure. One rabbit was irradiated once in a similar manner for eighty minutes and died twelve days later. One rabbit was irradiated once[35] through a field over the thorax and a second field over the thigh. Each field was exposed to the rays for eighty minutes, and the abdomen and neck were carefully shielded. The animal died nine days afterward. The hepatic region of three rabbits was irradiated[35] through two opposite fields, each field being exposed for eighty minutes. The animals died ten, ten, and eight days later, respectively. One of these three animals was given an intravenous injection of 10 per cent grape sugar solution two hours before death. The hepatic region of two rabbits was irradiated[35] once for eighty minutes through each of two opposite fields, and the animals died twelve and thirteen days later, respectively.

Clinical manifestations of gastric irritation or injury were not mentioned. Whether irradiation was directed to the liver or to the thorax and thigh (with liver and stomach shielded), the stomach of all the rabbits showed marked pathologic changes consisting of ulceration and hyperemia of the mucosa, degeneration of peptic glands, infiltration of the stroma with leucocytes and plasma cells, increased mitosis in the glandular epithelium which had not been destroyed, and sometimes proliferation of connective tissue. The ulcers in the gastric mucosa of some of the animals were round and their margins sharply defined, but other ulcers in the stomach of the same animals were irregular, sometimes extending to the serosa,

[32] Voltage equivalent to a parallel spark-gap of 39 cm.; focal-skin distance, 23 cm.; radiation filtered through 0.5 mm. of zinc; 2 ma.; size of fields, 6 by 8 cm.

[33] Voltage equivalent to a parallel spark-gap of 45 cm.; focal-skin distance, 23 cm.; radiation filtered through 0.5 mm. of zinc and 3 mm. of aluminium; 2 ma.; size of each of the two fields, 6 by 8 cm.

[34] Voltage, 180 kv.; focal-skin distance, 30 cm.; radiation filtered through 0.5 mm. of copper and 1 mm. of aluminium; current 4 ma.

[35] Coolidge tube; 180 kv.; focal-skin distance, 30 cm.; rays filtered through 0.5 mm. of copper and 1 mm. of aluminium; current 4 ma.

and appearing only as an accentuation of changes in other parts of the organ. The pylorus was occasionally swollen and edematous. Some of these ulcers were covered with or surrounded by blood-stained or blood-streaked mucus. In animals exposed to strong doses of roentgen rays the gastric mucosa was punctuated with fine capillary hemorrhages. The stomach of the rabbit which had been irradiated over the thorax and thigh showed thickening of the pylorus, a small shallow ulcer on the lesser curvature and several small, scattered erosions of the mucosa.

Portis and Arens (1924) tested the effect of short wave-length roentgen rays on the gastric secretion of two dogs.[36] From two to four weeks after the surgical preparation of a Pavlov pouch in each dog, preliminary determinations of the gastric secretion were made one hour before a test meal consisting of 200 gm. of raw meat, 50 gm. of toast or bread, and 250 c.c. of milk; the secretion was collected hourly for four hours after the test meal. The dogs were given a bone to chew on twice a week. The amount of gastric juice collected each hour was measured, titrated for free and total acids with 40 per cent sodium hydroxide;[37] the peptic activity was ascertained by the Mett method, but chloride determinations were not made. The gastric secretion of one dog was collected twice daily for fourteen days, after which a field 14 by 14 cm. over the thorax was irradiated on three successive days, the stomach being excluded from the field of irradiation.[38] The gastric secretion was then collected for from three to four weeks, after which the same dose of roentgen rays was given to the lower part of the abdomen (the stomach again excluded). After another interval of three weeks the same dose of roentgen radiation was given to the region of the stomach on three successive days.

After the same preliminary control determinations of the gastric secretion of the second dog, the same dose of roentgen rays, one-third of which had been given to the first dog on each of three successive days, was administered in one day to the thorax (the stomach excluded); the dose was repeated three weeks later. After an interval of four weeks the same dose was given in one day to the lower part of the abdomen, with the stomach excluded, and was repeated over the gastric region after another interval of four weeks. Before each exposure the secretion from the fasting stomach was collected; then the same test meal was given and the same determinations of the gastric secretion were made subsequently.

Irradiation of the thorax of the first dog produced essentially no effect on the free hydrochloric acid and total acidity.[39] Exposure of the lower part of the abdomen caused a marked decrease in the free and total acidity, while exposure of the gastric region alone caused an immediate, sharp rise in total acidity and free hydrochloric acid, followed promptly by a gradual decrease to, or nearly to, complete achylia. Substantially the same results were obtained in the second dog, except that the first irradiation was followed by a slightly more definite rise in the total acid and free hydrochloric acid levels, and that the decrease which followed the third irradiation was more rapid. Little effect on peptic activity was noted after irradiation of the thorax or lower part of the abdomen, but it was depressed after direct irradiation of the stomach. The decrease in pepsin did not become evident until after the acid had diminished greatly. The appetite of the dogs was influenced slightly after each exposure, but it soon returned to normal. Neither dog lost any weight during the four months of the experiment.

Brocq, Solomon and Oury (1924) studied the effect of direct irradiation of the stomach on the gastric function of dogs. Under anesthesia with morphine and chloroform and with careful asepsis, they made, in each of three dogs, a median, supraumbilical, laparotomy

[36] Age and weight not given.

[37] Reduced later to degrees of one-tenth normal.

[38] The dose of roentgen rays was: tube voltage, 200 kv.; focal-skin distance, 55 cm.; filter, 0.78 mm. copper over 1 mm. aluminium; tube current, 6 ma.; time not stated; energy delivered to the skin per hour, 600 "e" units (total of the three exposures, 1,800 "e" units); penetration, measured in paraffin; intensity at 10 cm. depth, 46 per cent of surface intensity.

[39] The authors stated that there was slight, transient increase, but their charts do not substantiate this clearly.

incision 5 to 6 cm. long, and caught with a clamp the greater curvature of the stomach at its most prominent point. A second incision, 1 to 1.5 cm. long, was made through the abdominal wall about 3.0 cm. to the left of the first incision, and the portion of the stomach held by the clamp was brought out through the second incision; the median laparotomy incision was then closed; the portion of the stomach protruding through the smaller incision to the left was sutured to the margin of the skin on each side, and a small opening 4 to 5 mm. was made in the gastric wall at this point. This yielded a perfectly continent orifice and yet gave ready access to the cavity of the stomach. As a test meal 250 c.c. of milk was used for one of the dogs; the other two received 200 c.c. of water and 50 gm. of chopped meat. The first test meal was not given until eight days after the operation, and all test meals were withdrawn one hour and forty-five minutes after ingestion by means of a soft rubber catheter introduced into the stomach through the fistula.

Dog 3: Operation was performed November 7, 1923. November 12, the total acidity was 91;[40] the free hydrochloric acid was 0. November 21, the total acidity was 200, the free hydrochloric acid was 0. December 7, the gastric region was irradiated.[41] A test meal given ten minutes later showed total acidity 296 and free hydrochloric acid 36. December 9, the total acidity was 161, and the free hydrochloric acid 21. December 13, irradiation[41] was again applied. December 19, the total acidity was 57, the free hydrochloric acid 0. December 26, the total acidity was 62 and the free hydrochloric acid 0.

Dog 4: February 4, the total acidity was 474 and the free hydrochloric acid 125. The animal was first irradiated[41] February 8. February 9, the total acidity was 631 and the free hydrochloric acid 0. February 14, the second irradiation[41] was given and February 22 the third; March 6, the total acidity was 511 and the free hydrochloric acid 277. March 10, the fourth irradiation[41] was given and March 13, the fifth. March 13, the total acidity was 547 and the free hydrochloric acid 66. March 16, the sixth irradiation[41] was given and March 20, the seventh. April 3, the total acidity was 394 and the free hydrochloric acid 0. May 1, the total acidity was 365 and the free hydrochloric acid 14.

Dog 5: May 17, the total acidity was 170 and the free hydrochloric acid 52. May 18, the first irradiation[41] was given. May 19, the total acidity was 250 and the free hydrochloric acid 117. May 24, the total acidity was 260 and the free hydrochloric acid 153. May 25, the second irradiation[41] was given. June 6, the total acidity was 120 and the free hydrochloric acid 30. June 12, the total acidity was 118 and the free hydrochloric acid 24.

Although the dogs were in equally good health, the gastric chemism was quite different at the outset (dog 3, achlorhydria; dog 4, hyperchlorhydria; dog 5, normal hydrochloric acidity), and irradiation had a different effect in each animal. In dog 3, hydrochloric acid, which was absent at first, appeared in the gastric secretion for a short time and again disappeared. In dog 4, the free hydrochloric acid fell sharply soon after irradiation, then fluctuated widely and finally dropped to zero or near the zero point. In dog 5, the free hydrochloric acid increased after irradiation, but later decreased greatly. In all three dogs irradiation was followed by a rise in total acidity and by a subsequent drop below the initial level. Brocq, Solomon and Oury concluded that the effect of direct roentgen irradiation of the stomach is to diminish the acidity of the gastric secretion. They mentioned the point that doses much stronger than those used in the treatment of human beings were used, but that strong doses were necessary to influence the gastric secretion of the dogs.

Ivy, McCarthy and Orndoff (1924) studied the effect on gastric secretion of roentgen irradiation of the thorax and abdomen, with the stomach excluded. Eleven dogs[42] were used for this purpose, and the surgical preparation of the Pavlov pouch, as well as the pre-irradiation and post-irradiation tests of gastric secretion, were conducted as in their earlier in-

[40] The values of total acidity and free hydrochloric acid were given in milligrams per 100 c.c. of gastric juice.
[41] 1000 R units (Solomon). Dog in dorsal position. Other technical factors were not mentioned.
[42] Age and weight not stated.

vestigation of the action of direct roentgen irradiation of the stomach. In two animals, 1 mg. of histamin was injected before irradiation, and again during the period of anorexia following irradiation, in order to ascertain if the gastric secretory mechanism itself was involved. Necropsy was performed on all but one of the animals that died. The intestine was examined microscopically.

The left thoracic wall of two dogs with Pavlov pouch was exposed once to roentgen rays[43] for seven minutes. Thirteen or fourteen days later the skin peeled and a shallow ulcer appeared, which persisted for about two months without healing. The irradiation did not cause symptoms, and the gastric secretion was not altered during the two months that followed.

The lower right side of the abdomen of two other dogs was irradiated once, thirty-seven minutes in one dog and thirty minutes in the other. Irradiation was followed by early vomiting, anorexia, and, in one dog, by diarrhea. The gastric secretion of one animal diminished greatly four days after irradiation and none was produced between the fifth and tenth days. Secretory function reappeared and increased slowly with return of appetite. The free hydrochloric acid and the total acidity also diminished, but such chemical variation was not great. Gastric secretion did not form in the Pavlov pouch of the second dog for eleven days after irradiation; it then reappeared and gradually returned to normal by the twentieth day, with return of appetite. The free hydrochloric acid and the total acidity diminished one-third in thirteen days and then slowly returned to normal. In spite of the tendency of the appetite to recover and of the stomach to recover its secretory activity, the animals became emaciated and cachectic, and died twenty-three and fifty days, respectively, after exposure. This decline was accompanied by renewed and progressive anorexia and by fresh depression in gastric secretion.

The entire abdomen of seven dogs was irradiated once[44] from the right side. Four of the animals vomited within a half to one hour; two vomited intermittently for two hours and one for four days. Partial anorexia was also present, and in five of the dogs there was increased secretion of gastric juice during the first two days after exposure to the roentgen rays. Partial or complete anorexia, decrease of gastric secretion and anacidity, beginning on the third day and continuing for two or three days, occurred in all the animals. The authors believed that the dogs recovered or died according to their vitality at the time of irradiation. Four dogs died from acute roentgen intoxication in from six to fourteen days. Of the three that recovered from the immediate intoxication, one died from hemorrhage after one month, one from fibrous pancreatitis after two months, and one from experimental intussusception after three months.

The entire abdomen of two dogs was irradiated once;[45] the immediate effects and influence on gastric secretion were the same as in the preceding group, except that gastric secretion did not increase at any time, and the symptoms of intoxication were mild.

Extensive pathologic changes were found in the intestine of most of the animals. The changes consisted in marked necrosis and autolysis of the epithelium lining the small intestine, and delay in the reaction of the fibroblasts.[46] The alterations produced by an erythema dose used for a dog and by that used in a human being were of the same kind, but differed in the degree of injury. The dose for the dog[47] produced complete sloughing in patches, thus exposing the surface of the intestine as deep as the muscularis mucosae. With the dose for man the villi were obliterated or denuded of epithelium, but complete sloughing did not occur. Extreme atrophy and fibrosis were noted in the pancreas of one dog, in which there was a marked increase in the secretion of gastric juice; the hypersecretion was ascribed to the un-

[43] Voltage, 110 kv.; skin-target distance, 30 cm.; filter, 1 mm. aluminium; current, 5 ma.; size of field, 6 cm. in diameter.

[44] The dose of roentgen rays was: voltage, 200 kv.; skin-target distance, 50 cm.; filter, 0.75 mm. copper and 1 mm. aluminium; size of field, 11 by 21 cm.; current, 5 ma.; time of exposure, 120 minutes.

[45] The same as in the previous group, except that the time of exposure was reduced to ninety minutes.

[46] For a more detailed description of the pathologic changes see under Intestine.

[47] Approximately three times greater than the erythema dose for human beings.

controlled acid stimulation of the intestine caused by absence of the neutralizing effect of pancreatic juice. The gastric secretion of most of the animals receiving strong doses increased for one or two days after irradiation of the extragastric portion of the abdomen, but after this the secretory activity diminished more than when the stomach was directly exposed. This secretory depression was attributed chiefly to the anorexia induced by irradiation, and the initial increase in secretory activity either to increased irritability of the intestinal mechanism concerned in gastric secretion, or to a reflex spasm of the pylorus from injury or irritation of the intestinal mucosa.

Dieterich and Rost (1925) studied the action of roentgen irradiation of the upper and lower parts of the body of two dogs, with the gastric and hepatic regions shielded from the rays. They also hoped to determine the relationship between any disturbance in gastrointestinal chemism caused by irradiation and radiation sickness which they had often noted after irradiation of the head. Gastric and duodenal fistulas were first prepared, and the animals protected from psychic disturbances. As a test meal the animals received, after fasting, 100 gm. of chopped meat, and the gastric secretion was obtained by opening the cannula a half hour and one hour after the test meal. The hydrogen ion concentration was determined according to Michaelis, and the pepsin according to Volhard. The fluid contents of the duodenum were examined after injecting into the efferent loop of the duodenum either Witte's peptone 1:30 or 30 c.c. of 25 per cent hydrochloric acid. With Witte's peptone a strong excretion of bile with the pancreatic juice was obtained, while hydrochloric acid yielded almost pure pancreatic juice, with only a slight admixture of bile. The hydrogen ion concentration of the bile and pancreatic juice, which was obtained free from food or gastric secretion, was determined by electrolytic methods, and quantitative estimation of the trypsin was made by the method of Volhard.

For irradiation the animals were placed on the back, with legs extended, and secured in this position. The head, gastric region and lower portion of the abdomen were exposed to roentgen rays[48] at intervals of from four days to approximately three months; only one field was irradiated at each session. The hypogastric region of one dog was exposed September 27, and October 2 and 26, 1923, to surface doses of 41, 62, and 83 per cent, respectively, and the head February 19, 1924, to a surface dose of 206 per cent. The head of the second dog was exposed July 18 and 25, 1923, to surface doses of 42 and 204 per cent, respectively, and the gastric region September 23 and December 9, 1924. No change clearly attributable to irradiation was found in the total and free hydrochloric acids of the gastric secretion after exposure of the head, gastric or hypogastric region, and the same was true of the hydrogen ion concentration of the duodenal fluid and the trypsin.

Radium. Werner (1907) studied the action of radium on the gastric mucosa through a laparotomy incision made under ether anesthesia. A capsule of radium[49] surrounded by a rubber finger cot and sterile gauze was placed against the serosa of the anterior wall of the stomach of two rabbits and maintained in position for thirty minutes. The animals were killed three and five days, respectively, after irradiation. In the dog killed five days after exposure there was degeneration, vacuolization and nuclear disintegration of the epithelium lining the glands of the part of the stomach exposed to radium, but such degenerative changes were not found in the surface epithelium. Werner concluded that the glandular epithelium is more sensitive to irradiation than that covering the surface of the mucosa.

Delbet, Herrenschmidt and Mocquot (1909) investigated the action of radium on the stomach of four dogs.[50] The radium unit consisted of 0.05 gm. of pure radium bromide in a

[48] Neo-Intensive apparatus with Coolidge tube operating at from 180 to 200 kv. measured with the voltmeter, or from 130 to 145 kv. measured spectrographically; filtration of 0.5 mm. of zinc and 3 mm. of aluminium; size of field, 20 by 20 cm.; intensity of current, 2.5 to 3.0 ma.; focal-skin distance, from 25 to 30 cm. Surface dose at different sessions from 41 to 206 per cent; depth dose at 8 cm. from 24 to 126 per cent.

[49] The quantity of radium and the character and thickness of the capsule containing it were not mentioned.

[50] The age, sex and weight of the animals were not given.

cylindrical glass tube within a hermetically sealed tube of silver 0.5 mm. thick. The radium was at one end of the tube, and while its theoretic activity was 2,000,000 its useful activity was only 10,400. The other end of the container was equipped with a ring, by which it was fixed to the wall of the stomach; thus the end containing the radium was free to move in a circle around the point of attachment, which was near the juncture of the upper two-thirds and the lower third of the greater curvature, toward its anterior aspect. Gastrotomy was performed twice on each dog: one to place the radium tube, and the other in twenty-four hours to withdraw it. The animals were killed twenty-four hours, eight days, fifteen days, and five weeks, respectively, after irradiation.

Twenty-four hours after exposure there were no macroscopic lesions aside from the operative incision; there was, however, a diminution in the number and height of the rugae around the point of attachment of the radium tube. Eight days after irradiation six points of ecchymosis were noted in a zone 3 cm. in diameter corresponding to the site of the radium tube. Fifteen days after irradiation the mucosa in the prepyloric region was gray; that in the cardiac region was pink and characterized by smaller folds. About 2 cm. from the site of the radium capsule, on the pyloric side, a semilunar band 6 to 7 cm. long and 1 to 2 cm. wide extended transversely to the axis of the stomach. The mucosa in the region of this band was dull and showed a fine hemorrhagic stippling, in which was a sharply defined ulcer 4 mm. in diameter, with a yellowish-gray base, on the posterior aspect of the organ. At a short distance was a small yellowish granule. Five weeks after irradiation there was a zone of hyperemia 7 by 1.5 cm., and 3 cm. distant from the site of the radium capsule, on the cardiac side. The folds of mucosa in this zone were broad, low and edematous, and were characterized by hemorrhagic stippling, especially between the folds and around the patches of superficial necrosis. These lesions could not possibly be due to simple trauma. The site of the lesions in the different animals, toward the pylorus in one and toward the cardia in the other (with respect to the site of the radium tube), indicates that the tube did not rotate around its point of attachment, but assumed a proximal or distal position, according to the manner of its introduction.

Paraffin sections[51] of the stomach of each of the four dogs were stained with hematoxylin, amantia-eosin, mucicarmine, and Podwyssotski stain. Twenty-four hours after irradiation, in the region underlying the radium tube and as far as 3 cm. from it, the surface epithelium and that which lined the crypts was normal, except that the nuclei were stained more deeply than normal. The glandular tubules also were normal, but there was hypertrophic thickening of the interglandular connective tissue, with a few migrating cells. The muscularis also was normal, but the submucosa was greatly thickened by serous infiltration, which might possibly have been due to surgical trauma. The capillaries were dilated, and interstitial hemorrhages were noted here and there. Eight days after irradiation only the operative lesions were found at the site of the radium capsule, but 2 cm. distant there was a small hemorrhagic extravasation under the surface epithelium, around the mucous calices of the glands. The only other pathologic change was dilatation of the vessels. The three coats of the gastric wall were quite normal 3 to 6 cm. from the site of the radium capsule.

Fifteen days after exposure the lesions in the stomach were limited to a dull semilunar band, with hemorrhagic stippling, most marked around a small ulcer 4 mm. in diameter. The volume of the glands in the zone of dullness and stippling away from the ulcer was diminished by rarefaction of the chief cells, and the interglandular tissue was increased by fibroblastic hyperplasia and by moderate leucocytic infiltration. The parietal cells at the bottom of the glandular tubules were increased in number, and the mucous cells of the crypts tended to resemble the parietal cells by their affinity for amantia-eosin. Some of the nuclei had disintegrated. The ulcer corresponded to the position of the radium. Even at 1 cm. from it the

[51] The pieces of tissue had been fixed in sublimate.

crypts were obliterated, and 2 to 3 mm. from the ulcer the glandular coat was thinner than usual. At the level of the ulcer, which was lined by young connective tissue infiltrated by polymorphonuclear leucocytes, the muscularis mucosae was broken and the submucosa slightly edematous. From the normal portion of the mucosa toward the ulcer the mucous cells were gradually replaced by acidophil cells, which increased in number, became vacuolated and secreted less and less mucus. The glands became true cavities, well apart, and were reduced to mere hollow shells lined with swollen and vacuolated, low cubical or crescent-shaped epithelial cells. The parietal cells predominated in number, volume and situation. The epithelium was absent from some of the glands, which sometimes opened out widely, while others were full of desquamated and vacuolated epithelium, with lightly staining nuclei. There was no sign of phagocytosis.

Five weeks after irradiation the hemorrhagic zone represented a broad band of epithelial destruction with beginning regeneration, and the margins were sharply defined. The border of the ulcer was composed of papillomatous folds of epithelium rising above the surrounding surface or showing infundibula of bizarre shape, all lined with high mucous cells. The glandular tubules underlying the edge of the ulcer had all formed recently. The mucosa 3 mm. away from the villous border was wholly normal. The papillae and crypts were lined entirely by mucous cells deeply stained with mucicarmine. The newly formed glands were lined with cells which still gave the reaction of mucous cells, and numerous mitotic figures were seen in the advancing edge of mucous cells. Half of the base of the ulcer, composed of young, vascular, connective tissue infiltrated by leucocytes, rested on the submucosa; the other half rested on the muscularis. This connective tissue proliferation was a more prominent feature than it was fifteen days after irradiation. The vessels in the muscularis and submucosa were dilated.

Delbet, Herrenschmidt and Mocquot summarized their data by saying that the three varieties of cells of the gastric mucosa are influenced differently by penetrating radium rays; that the chief cells may secrete mucus for a time and then disappear; that the parietal cells undergo hypertrophy, replace the chief cells, lose their zymogen granules, but remain acidophil and slowly disappear; that the mucous cells abound, later lose their property of secreting mucus and disappear; that the chief cells are the most, and the mucous cells the least, sensitive to radiation; that while the chief cells are undergoing degeneration, the parietal cells and the interglandular connective tissue behave as if stimulated, and that their results tended to establish the fact that the radiosensitiveness of each variety of cell is characteristic of or specific to it.

Lazarus-Barlow (1922) irradiated the entire body of twenty frogs, twenty-eight rats, fifteen rabbits and nine cats with 5 gm. of hydrated radium bromide. A description of these experiments will be found elsewhere (see page 10).

In proportion to the exposure or survival after exposure the epithelium of the secreting portion of the stomach of all the animals showed a progressive tendency to mucoid degeneration, disintegration, and desquamation, with vesiculation of its nuclei. In pronounced cases the secreting and investing epithelium had disappeared almost completely, and the mucosa ultimately consisted of a gelatinous, mucoid or edematous, poorly cellular stroma, with hemorrhagic extravasation. Masses of chromatin, probably representing mitosis, were occasionally found. Goblet cells were absent or few. Little mucus formed in the less severe cases, but there was a large amount when exposure or survival after irradiation had been prolonged. Regardless of the duration of exposure, the destruction was greatest when the survival was longest.

Analysis of Experimental Data

Roentgen Rays. The results of the foregoing experiments may appear slightly confusing because the technical conditions varied with the point of view underlying the

experiments and because irradiation was seldom confined to the stomach, but generally included a greater or smaller portion of the intestine and other organs, such as the spleen, liver and pancreas. In at least two cases (Szegö and Rother, Miescher) the investigation was conducted on a single dog, while in the others control experiments were not uniform. Regaud, Nogier and Lacassagne (1912) were apparently the first to investigate, experimentally, the action of roentgen rays on the digestive tract. So far as the stomach is concerned, their studies indicate that the epithelium of the gastric mucosa is only moderately sensitive to irradiation, less so than that of the small intestine; that the epithelium of the gastric fundus is more sensitive than that of the pyloric region, and that acute or chronic lesions may be produced according to the dose and the length of survival or observation. These conclusions have, in the main, been sustained. A careful review of the doses of roentgen rays, the number of separate exposures, the intervals between them and the period of survival or observation following them indicate that single small doses, that is, doses within the therapeutic range for human beings, have no effect on the quantity or quality of gastric secretion. Szegö and Rother (1921) stated that small doses have no effect on gastric secretion, and Ivy, Orndoff, Jacoby and Whitlow (1923) asserted that they were unable to find any dose the effect of which was to increase the secretion of gastric juice. Szegö and Rother claimed and submitted data to show that large doses increase the daily output of gastric juice, but this increase was of short duration and may well have been associated with the presence in the stomach of barium with which the organ had twice been filled before irradiation. It is unfortunate that these experiments should have lost so much value by being conducted on a single animal.

The experiments in which the action of radiation on the daily output of gastric secretion is mentioned show that the general effect of strong doses[52] of roentgen rays on the stomach is to decrease the daily output of gastric juice, the total and free hydrochloric acids and the pepsin content of the secretion. In the experiments of Szegö and Rother (1921), Miescher (1923), and in some of those of Ivy, McCarthy and Orndoff (1924), the quantity of gastric secretion increased shortly after strong irradiation and continued irregularly for from a few days to two weeks. After this the quantity of juice secreted fell below normal, oscillated above and below this low level for a time, and then slowly returned to or slightly above the preirradiation level. Each succeeding exposure caused a similar reaction, but after from two to four exposures the immediate rise in secretory activity following exposure did not reach the initial normal level and the succeeding fall was lower and lower. The early, transient increase in the quantity of secretion noted by Szegö and Rother (1921), Miescher (1923), and Ivy, McCarthy and Orndoff (1924) after large doses[52] of roentgen rays is not easy to explain; nor is it less difficult to reconcile this observation with the inability of Ivy, Orndoff, Jacoby and Whitlow to cause a similar increase by any arrangement of dosage; according to them large doses always produced secretory depression or abolished the secretion altogether.

The belief of Szegö and Rother that the immediate transient rise in gastric secretion observed by them was a manifestation of gastric stimulation by the rays rests on an insecure foundation. Miescher was careful to warn against such an assumption, and his warning is emphasized by the experiments of Ivy, McCarthy and Orn-

[52] Doses beyond the therapeutic range for human beings.

doff (1924). The object of these experiments was to ascertain the effect on gastric secretion of irradiation directed to the thorax or to the lower part of the abdomen, with the stomach excluded.[53] Irradiation of the thorax (stomach excluded) had no effect on gastric secretion. Irradiation of the right lower part of the abdomen (stomach excluded) of two dogs caused the output of secretion to diminish, without any preliminary rise. In seven dogs irradiation of the abdomen was followed in five by an increased secretion of gastric juice for two days, after which the amount fell below normal. Moreover, these authors pointed out that the decrease in secretory output after extragastric, abdominal irradiation was greater than after direct irradiation of the stomach. In view of such results, it is impossible to accept Szegö and Rother's hypothesis that direct stimulation of the secretory cells of the stomach by the rays accounts for the transient increase in gastric secretion after irradiation. The explanation advanced by Ivy, McCarthy and Orndoff is nearer the mark, as according to them the initial increase in secretory activity is due either to increased irritability of the intestinal mechanism concerned in gastric secretion or to a reflex spasm of the pylorus from injury or irritation of the intestinal mucosa. The majority of the animals used in the foregoing experiments suffered varying degrees of gastric and intestinal injury, as is shown by the more or less severe clinical symptoms that followed irradiation, such as anorexia, nausea, vomiting, diarrhea (sometimes bloody), loss of weight, cachexia and death. Several of the experiments also furnish ample evidence of intestinal injury. In all probability, the initial and transient increase in gastric secretion is to be regarded as an effort on the part of the secreting cells to counteract the noxious influence of the rays, such effort appearing during the early phase of reaction, to disappear and be replaced by secretory depression.

Nearly all the experiments agree in showing that irradiation causes the total acidity and free hydrochloric acid to diminish, and to remain low for a time. Later the total and free acids return to normal. The depressing effect varies in degree and duration according to the dose and apparently also according to the status of the acidity before irradiation. Brocq, Solomon and Oury (1924) pointed out that in one of their dogs hydrochloric acid, which was absent from the gastric secretion before irradiation, appeared for a short time after exposure to roentgen rays. Miescher (1923) made the interesting observation that a traumatic ulcer, which had formed at the point of union between the gastric fistula and the skin and which, before irradiation, increased steadily in size, healed after two exposures had reduced the acidity of the gastric juice to a low level. This may well explain the healing action of radiation on peptic ulcer. (Clinical considerations, page 35.)

The experiments in which the behavior of pepsin was observed all show that pepsin is not easily affected by irradiation. Repeated exposure of the stomach is necessary before any appreciable change in the pepsin is produced. This indicates that the cellular mechanism responsible for the secretion of pepsin is more resistant than the cells which secrete or elaborate the gastric acids. However, strong, and especially repeated, irradiation causes the pepsin to diminish greatly. The diminution lasts longer and the regeneration is slower than is the case with total and free hydrochloric acidity and daily output of secretion. That the peptic depression may be related to the acidity of the secretion was suggested by Portis and Arens, who pointed out that

[53] The first step in the experiments was the surgical preparation of a Pavlov pouch.

the decrease in pepsin does not become apparent until after the acid has diminished greatly. In the absence of more specific and conclusive data the point must remain unsettled. Moreover, the peptic activity of the stomach is influenced only by direct irradiation of the organ; Portis and Arens remarked that little effect on peptic activity was noted after irradiation of the thorax and lower part of the abdomen. This is corroborated by Ivy, Orndoff, Jacoby and Whitlow who, having irradiated only a half of the Pavlov pouch of one dog, found the production of acid and pepsin to have ceased only in the irradiated half.

Regaud, Nogier and Lacassagne (1912), Ghilarducci (1916), Szegö and Rother (1921), and Dawson[54] (1925) included in their report a description of the pathologic changes in the stomach and intestine. These descriptions show that strong doses of roentgen radiation act on the stomach by causing degeneration of the gastric epithelium. The chief cells appear more vulnerable than the parietal cells, but, according to Dawson, some of the chief cells that appear to have preserved their histologic integrity are functionally inert. The epithelial cells undergo vacuolation and cytolysis, and the pepsin granules are set free in the lumen of the injured glands. Such acute cellular degeneration is accompanied by hyperemia or petechial hemorrhages in the mucosa, and by leucocytic infiltration. Ghilarducci has shown that even severe ulceration to the extent of perforation may be produced. Later the interglandular connective tissue increases irregularly, and groups of glandular tubules are crowded together and so separated from other groups as to give an appearance of islands of tubules. The proliferation of connective tissue extends deeply into the mucosa, giving it a narrow, sclerosed appearance. Szegö and Rother stated that the mucosa of the irradiated portion of the stomach was only half as thick as that of the unirradiated portion, and that such sclerotic atrophy affected the lamina propria, the muscular and submucous coats. Dawson did not observe any infiltration of the mucosa by leucocytes, and the fibroblasts showed hypertrophy but no proliferation. Moreover, he added that all the pouches of Pavlov which subsequently recovered their normal function were found histologically complete. This would indicate, as one would expect, that the dose of radiation plays an important part in the degree of injury produced, that the gastric mucosa can withstand fairly strong doses, but that doses beyond the limit of tolerance may cause extensive and permanent injury.

Tsukamoto's investigation was related primarily to the action of roentgen rays on the liver and general metabolism, but it also showed marked degenerative and ulcerative changes in the stomach. Considering the extreme doses often employed, such injury is not surprising. Some of the ulcers described by Tsukamoto appear to have been chronic lesions unrelated to irradiation.

So far as the intestine is concerned, the experiments of Regaud, Nogier and Lacassagne (1912), Szegö and Rother (1921), Ivy, McCarthy and Orndoff (1924) and Oury (1925) concur in showing that the mucosa of the intestine, especially the small intestine, is much more sensitive to radiation than the mucosa of the stomach. Marked degenerative and destructive changes, sometimes leading to perforation, nearly always followed irradiation and were generally associated with clinical manifestations of severe intestinal irritation, such as diarrhea, emaciation, cachexia and death. The intensity of these manifestations and of the pathologic changes found

[54] Dawson reported separately the pathologic changes in the stomach and intestine of the dogs irradiated by Ivy, Orndoff Jacoby and Whitlow.

at necropsy varied with the dose. The intestinal and general disturbances resulting from doses within the therapeutic range for human beings were comparatively slight. Thus the dogs irradiated by Portis and Arens (1924) had only slight anorexia, but they soon recovered their normal appetite and did not lose weight, in sharp contrast with most of the other experiments, in which much stronger doses were used and many animals suffered severely and died. Moreover, microscopic examination of the intestine of most of these animals showed great destruction and desquamation of the epithelium, atrophy of the glands of Lieberkühn, and leucocytic infiltration and proliferation of the interglandular connective tissue. In some cases (Regaud, Nogier and Lacassagne) the intestinal mucosa had been injured so greatly that perforation occurred. A more detailed description and analysis of the injurious effect of excessive irradiation on the bowel will be given later. It is mentioned briefly here because it is partly responsible for the severe systemic reaction which followed irradiation of most of the animals, and because it probably also played a considerable, although less tangible, part in the behavior of the gastric secretion. As has been noted, irradiation usually was not confined to the stomach, but a greater or smaller portion of the intestine and other abdominal structures was included. For this reason the part that irradiation of the stomach, intestine or other abdominal structures played in the ensuing behavior of the gastric secretory function cannot be accurately determined.

Radium. The first experimental investigation of the action of radium on the stomach was made by Delbet, Herrenschmidt and Mocquot (1909), whose interest related to the organic rather than to the functional effect of radium. Their radium container, which provided only moderate filtration,[55] was fastened by one end to the inner wall of the stomach through a gastrostomy incision, and was withdrawn after twenty-four hours. The pathologic changes noted under these conditions indicate that a certain proportion of the radiation consisted of beta rays. The hemorrhagic stippling and extravasation suggest that the blood vessels suffered early, but this point is not specifically mentioned. Cellular degeneration of the epithelium lining the glandular tubules, edema, hyperemia, leucocytic infiltration of the mucosa, and finally ulceration opposite the point of greatest radiation intensity, marked the degenerative stage of tissue reaction. Later, proliferation of the interglandular connective tissue and regeneration of the glands themselves marked the reparative stage. According to Delbet, Herrenschmidt and Mocquot, the chief cells are the most sensitive of the gastric cells to radium, as they have been previously shown to be to roentgen rays. The chief interest of these experiments is in connection with the use of radium in the treatment of gastric lesions.

The effect on the stomach of exposing the entire body of frogs, rabbits, rats and cats to a large quantity (5 gm.) of radium, as described by Lazarus-Barlow, is of the same general character as that observed by Delbet, Herrenschmidt and Mocquot, except that the effect is more diffuse and not limited to any one region. Under these conditions, the pathologic alterations varied with the duration of exposure or survival from mucoid degeneration, nuclear vesiculation, and desquamation to almost complete disappearance of the gastric epithelium. The stroma of the mucosa became gelatinous, mucoid or edematous, and hemorrhagic extravasations were

[55] Glass and 0.5 mm. of silver.

scattered through it. This pathologic picture represents only the early, or inflammatory, phase of the reaction, because the period of survival was a matter of hours or a few days. The subsequent changes constituting the reparative phase of reaction were not observed.

It is obvious that the action of a small quantity of moderately filtered radium or of a large quantity of heavily filtered radium differs chiefly in extent and depends largely on the conditions of exposure. Radium in contact with the mucosa causes only a local effect, the degree of which depends on the quantity, the filtration and the duration of irradiation. On the other hand, general exposure of the organ to a large external source of radium, from which the beta rays have been absorbed by filtration, causes diffuse degeneration of the secreting epithelium, edema and hemorrhagic extravasation in the mucosa. These, however, constitute only the initial phase of the reaction, and it is probable that examination of the stomach several weeks or months later would show either complete or partial regeneration or permanent destruction of the mucosa with connective tissue replacement of the elements destroyed.

Clinical Considerations

Roentgen Rays. It was but natural that the inhibitory action of roentgen rays should be submitted to the test of clinical requirements. Bruegel (1916) was apparently the first to undertake such investigation on human beings. He irradiated, in cases[56] of simple hyperchlorhydria, hyperacidity associated with chronic ulcer, and hyperacidity or anacidity, with moderate doses of rays of medium quality and also with moderate doses of more penetrating radiation. The free hydrochloric acid and total acidity decreased more rapidly in cases of simple hyperchlorhydria than in cases of hyperacidity associated with ulcer. Very small doses never increased the acidity of the gastric secretion if there was hyperacidity or anacidity. Bruegel, in 1917, reported having treated more than ninety cases of hyperacidity. He cited four cases with excessive acidity of the gastric juice and peptic ulcer, in which great improvement followed exposure of the stomach to roentgen rays. Reduction of acidity was noted in most cases of simple hyperchlorhydria, but this was short-lived unless irradiation was repeated several times. He also reported improvement in symptoms and reduction in acidity if there was spasm of the esophagus, cardia or pylorus, but no effect in cases of hypoacidity or anacidity.

Miescher (1920) applied at one time, to twelve human subjects, 15 X units[12] of roentgen rays of unspecified quality, filtered through 4 mm. of aluminium, to a single field over the gastric region. The free hydrochloric acid and total acidity decreased in seven cases; there was no change in three cases, and the free hydrochloric acid increased in two cases. Miescher thought the dose too small to cause a uniform decrease in the acidity of the gastric secretion. Wachter (1921) also investigated the action of roentgen rays on the gastric acidity of human beings. The free hydrochloric acid and total acidity diminished in six of eight cases in which the initial acidity was normal, and the fall was greater in free hydrochloric acid than in total acidity. An increase in acidity was noted in two cases. In four cases of hyperacidity the free hydrochloric acid and the total acidity fell proportionately, but the rate of reaction

[56] The number of patients is not stated.
[12] Kienböck units.

varied. The depressing effect of irradiation was slow to appear in one case in which excessive acidity was associated with ulcer. Free hydrochloric acid made its appearance in four cases of nervous dyspepsia, the gastric juice of which had previously been devoid of free hydrochloric acid, but Wachter did not attempt to explain this chance observation, which he regarded as evidence of a stimulating effect of irradiation. Irradiation sometimes caused transient, cramp-like pain around the stomach or abdomen and nausea or vomiting, but these symptoms disappeared rapidly. This investigator was unable to perceive any difference in effect between a dose given in four quarter-sessions and a similar dose given in a single session.

Kolta (1924) exposed to roentgen rays the gastric region in thirty cases of hyperacidity without ulcer. The free hydrochloric acid and total acidity decreased for a short time in thirteen cases, and for a "considerable period" in six; this was accompanied by improvement in symptoms. An increase in acidity was noted in a few instances.

Bensaude, Solomon and Oury (1925) tested the action of roentgen rays on gastric acidity by irradiating[58] the gastric region, in twenty-one cases, once or twice a week for from eight to ten weeks. The stomach was always fasting, and each exposure was preceded and followed by a test meal,[59] which was withdrawn after an hour and submitted to acid estimations by the method of Robin and Boussigault. A single dose caused the acidity to fall within an hour in a third of the subjects, but the fall in acidity lasted only a short time and the acids were normal again the next day. After each subsequent exposure the acidity fell lower until irradiation was discontinued, when it gradually returned to normal. After several exposures the acidity fell rapidly in 55 per cent of the subjects. The fall in free hydrochloric acid was greater than that in total acids. The pepsin was affected more slowly but more uniformly than the acids. Oury (1925) made twenty-six exposures in twelve cases of proved or latent ulcer or of mere functional disturbances. This was preceded and followed by gastric lavage and a test meal under similar conditions and at the same time on two successive days. No immediate change in gastric acidity was noted after eighteen of the exposures, but the free hydrochloric and total acids decreased within an hour in a third of the cases; acidity returned to normal in twenty-four hours. In eleven of twenty other cases, in which the stomach was irradiated weekly or biweekly, there was a marked fall in free hydrochloric and total acids; a moderate decrease in acids was noted in five cases; there was no change in three, and the acids increased in one case. The total acids returned to normal more rapidly than the free hydrochloric acid. The effect of roentgen rays on the acidity of the gastric secretion was greatest in the cases in which the gastric acidity was highest at the outset; no effect was noted in cases of low acidity or achlorhydria.

Lenk and Holzknecht (1926) stated that a single exposure of the stomach to roentgen rays is followed by a transient fall in gastric acids, but that the acids rapidly return to the initial level. They stated further that three or more exposures are followed by a marked and lasting fall in gastric acids.

Simonetti (1923) exposed the gastric region to roentgen irradiation in eleven cases, in four of which the patients were suffering from sequelae of encephalitis lethargica, five from pleuritis, one from carcinoma of the stomach and one from

[58] 500 Solomon "R" units given at each session.
[59] Water, 200 c.c.; stale bread, 60 gm.; half the white of one egg.

enterocolitis. The exposures varied in duration from three to seven minutes, and were made from five to fifteen minutes after an Ewald test meal.[60] The gastric contents were withdrawn an hour later; the total acids were determined by the Topfer method; the free hydrochloric acid, by the alizarin method, and the pepsin by the Hammerschlag method. The total acids increased in ten cases and diminished in three of the eleven cases in which thirteen irradiations were given. The free hydrochloric acid increased in seven cases and diminished in the remainder, and the pepsin increased after eight of twelve tests. Simonetti regarded this as evidence of secretory stimulation by the rays, but he did not mention how long the effect lasted.

From the foregoing it appears that the action of therapeutic doses of roentgen rays on the gastric secretion of human beings is essentially the same as, although less marked than, that which occurs after larger doses given to animals. The only difference is that the inhibitory effect is less constant and less pronounced, which is readily accounted for by the difference in dose. The effect of gastric irradiation in most cases is a fall of the total and free hydrochloric acids. According to Bensaude, Solomon and Oury, Oury, and Lenk and Holzknecht, the fall is transient after single exposures, and the acids return to normal within twenty-four hours. The acidity decreases more and more after each subsequent irradiation, and the effect is more lasting. A slow return to normal occurs after the irradiations have been discontinued. The fall in the free hydrochloric acid is greater than in total acids, according to Bensaude, Solomon and Oury. Wachter found this to occur only in cases in which the initial acidity was normal, but the decrease in free hydrochloric and total acids was proportionate in cases of initial hyperacidity. Bruegel and Oury agree that the fall in acids was greatest when the initial acidity was highest, and that little or no effect was noted when the gastric acidity was low at the outset or when the secretion did not contain acids. The observations of Bruegel and Wachter indicate that roentgen rays have less influence on gastric acids when the excess of acids is associated with ulcer, possibly because the irritation caused by the ulcer or by the condition responsible for the ulcer is also responsible for the continued excessive secretion of acids.

Bruegel tested the action of small, so-called stimulating doses of roentgen rays on gastric secretion, but did not observe any increase in acidity. Bensaude, Solomon and Oury, and Lenk and Holzknecht found that the acidity diminished in most cases after ordinary therapeutic doses, but when it did not diminish it remained at the initial level. On the other hand, an increase in free hydrochloric acid was noted in a few cases by Wachter, Miescher, Kolta, and Oury; this was exceptional, and the acidity of the gastric secretion in the majority of their cases decreased. Simonetti alone found that the total acids increased following ten of thirteen irradiations of the gastric region in eleven cases, that free hydrochloric acid increased after seven irradiations, and pepsin after eight of twelve irradiations. Wachter, Miescher, and Kolta did not attempt to explain the occasional increase, but Simonetti regarded the increase in free hydrochloric and total acids, noted in the majority of his cases, as evidence of secretory stimulation by the rays. No change in acids in cases of achlorhydria or anacidity was noted by Oury, while Wachter recorded the interesting observation of two cases, in which gastric juice had been devoid of acids in spite of the administration of 10 drops of hydrochloric acid three times a day, and in the gastric

[60] 50 gm. of bread and 400 c.c. of water.

secretion of which free hydrochloric and total acids appeared and increased rapidly after exposure of the stomach to roentgen irradiation.

In view of the evidence furnished by animal experiments and by most of the clinical data, the idea of a possible, direct stimulating effect of roentgen rays on the gastric epithelium is hardly tenable. It appears more likely that the increase in acidity, noted in a few cases after irradiation, is due to other unexplained factors. Simonetti's observations are so exceptional that they cannot be accepted without confirmation; they cannot be explained by a comparison of his technical conditions with those of others.

Radiotherapy for Gastric Ulcer. It is worthy of note that the symptoms associated with excess of acid in the gastric secretion or with ulcer of the stomach, such as pain, hemorrhage, burning, and loss of weight, were generally relieved in cases in which the acidity was reduced by irradiation. Kodon (1913), Wilms (1916), Bruegel (1917), Menzer (1919), Bryan and Dormody (1921), Lenk (1921), Kottmaier (1922), Piot (1922), Schulze-Berge (1922), Gunsett and Sichel (1923), Matoni (1923), Menzer (1923), Strauss (1923), Kolta (1924), Heuser (1924), Bensaude, Solomon and Oury (1925), Oury (1925), Lenk and Holzknecht (1926), Schiller and Altschul (1927), and others have reported many cases of simple hyperacidity or peptic ulcer with excess of gastric acids, hemorrhage, and loss of weight, in which the symptoms abated or disappeared after roentgen treatment of the stomach. It is true that the diagnosis of peptic ulcer was often based on clinical data only, but definite roentgenologic evidence of ulcer was obtained in many cases, and in others the presence of ulceration had been established by antecedent exploratory or other operation. Improvement in the condition of patients was characterized by cessation of pain and hemorrhage, decrease of gastric acidity, and increased weight. Such improvement is the more noteworthy because, at least in some cases, the symptoms had recurred after a previous attempt to relieve the situation by surgical measures or they had continued in spite of prolonged internal medication.

As stated by Menzer (1923), the results claimed by some of the foregoing authors are rather optimistic. Nevertheless, the number of cases reported and the degree and duration of improvement shown deserve consideration. Matoni's report covers 140 cases, in 77 per cent of which the patients were said to have been cured, 13.5 per cent improved, and 9.5 per cent not improved. Strauss treated fifty-two patients by roentgen irradiation, all but five of whom were regarded as improved, but Strauss did not consider the improvement permanent. Lenk and Holzknecht reported having treated more than fifty patients with proved peptic ulcer, forty-three of whom were observed over long periods; twenty-one had remained well; thirteen still had slight symptoms or recurrence of symptoms; five had shown only slight improvement, and four had not been influenced favorably by the treatment.

Radiotherapy for Spastic Disturbances of the Esophagus, Cardia and Pylorus. Attention has been directed to the beneficial action of roentgen irradiation on spastic disburbances of the esophagus, cardia, pylorus, and the stoma of gastroenteric anastomoses. Wilms (1916) cited two patients with cramp-like pain in the region of the pylorus, who were considerably relieved by roentgen irradiation. Menzer (1919) recorded two cases of gastrospasm (one patient with gastric ulcer and the other, a child four and a half years old, with pylorospasm); the patients derived distinct

benefit from irradiation. Subsequent roentgenologic examination showed complete disappearance of spastic phenomena, and the patients were correspondingly improved. Lenk reported disappearance of symptoms and return of function in thirteen of nineteen cases in which there was spastic interference with the function of a gastroenteric stoma. Observations on some of these patients for one and a half years did not disclose recurrence.

The improvement or cure in most cases of peptic ulcer and spastic disturbances has been attributed to the reduction in gastric acidity resulting from gastric irradiation. This explanation is favored by Bruegel, Wilms, Bryan and Dormody, and Lenk. Wilms and others, such as Gunsett and Sichel, and KORBSCH (1926) believed that irradiation acts partly or largely on the lymphocytes which form a part of the inflammatory deposits around the ulcer or other lesions responsible for the symptoms. On the other hand, HEUSER (1924) and Lenk and Holzknecht felt that the cessation of hemorrhage could be accounted for only by the effect of irradiation on the spleen, by virtue of which the coagulability of the blood is increased. Strauss alone has invoked a change in hydrogen ion concentration of the gastric juice to explain the favorable effect of irradiation on peptic ulcer. On the whole, it seems likely that one or more of these factors may play a part in the improvement, but in spite of Strauss's contention, the influence of hydrogen ion concentration is far from established.

Relief from pain associated with simple hyperchlorhydria, ulcer or spastic phenomena has been one of the outstanding features of roentgen treatment in most of the cases cited. The reduction of gastric acidity after irradiation is undoubtedly sufficient to account for the cessation of pain due to excessive acidity. But in peptic ulcer mere lowering of gastric acidity may not be sufficient; it is probable that a destructive effect on lymphocytes forming part of the leucocytic infiltration around the ulcer may be a more potent factor than the change in acidity. However, neither of these factors appears to account adequately for relief from pain in certain forms of gastrospasm, such as pylorospasm in children. Although possible, there is little tangible evidence of direct action of the rays on vagus terminations to provide a satisfactory explanation.

Radium. WINTERNITZ (1911) was the first investigator, and seems also to have been the last, to note the action of radium on gastric chemism and motor function. He added radium emanation water to test meals given to normal subjects and to patients with hypoacidity or hyperacidity, but found no change in the acid or peptic content of the gastric secretion, or on gastric motility.

Conclusions

Roentgen Rays. The animal experiments undertaken to determine the effect of irradiation on the stomach indicate that the gastric mucosa is moderately sensitive to roentgen and radium rays, but less so than that of the intestine. They show that while small or moderate doses of radiation have little or no effect on gastric secretion or on the mucous lining of the organ, large doses cause diminution of the daily output of secretion, the free hydrochloric and total acids and the pepsin. The degree and duration of this effect depend on the total irradiation, whether given at one time or at repeated sessions. The status of the gastric acidity before irradiation appears to have an important bearing on the effect produced. The inhibitory effect on gastric

acidity is greater in cases of simple hyperacidity than if excess of acids is associated with ulcer. The output of secretion and the acidity tend to return to normal after irradiation has been discontinued. The acid content of the gastric juice increases occasionally soon after exposure, but this disappears rapidly and can hardly be regarded as a result of direct stimulation of the gastric epithelium. The pepsin is affected slowly; to depress peptic activity requires strong or repeated exposure of the stomach. The resulting peptic depression is more lasting and the subsequent regeneration slower than is the case with acidity.

The functional effects are accompanied by and are due to pathologic changes in the mucous membrane of the stomach, which consist of degeneration of the epithelium, hyperemia and hemorrhage, leucocytic infiltration of the stroma, followed by regeneration or more or less marked proliferation of the connective tissue and atrophy of the mucosa.

Clinically, the effect of irradiation on the stomach is essentially the same, except that the influence on function is less pronounced and less constant. This may be explained by difference in dosage. The symptoms which accompany simple hyperacidity and excessive acidity associated with chronic peptic ulcer often subside or disappear, apparently due to reduction of the acidity and destruction of the lymphocytes infiltrating the margins of the ulcer.

Radium. Radium applied directly to the gastric mucosa from within has an intense local effect. Extreme degeneration of the epithelium, with hemorrhagic extravasation or even ulceration may result. The action of radium rays directed to the stomach from an external source is the same as that of roentgen rays.

To be continued.